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Heavy metals and carcinogenesis: a review

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Abstract

There has been a growing recognition regarding heavy metal toxicity owing to their position in cancer induction. The study is linked to heavy metals like titanium, arsenic, beryllium, cadmium, lead, mercury, nickel and radium. A meta-analysis was compiled using PubMed to determine existing exposure channels, forms of cancers caused, and treatment interventions for the metals. It was planned to lead potential study activities linked to heavy metals and cancer.

Keywords: heavy metals, toxicity, carcinogenesis

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Introduction

Heavy metals toxicity represents major health issues in humans. These components have the potential to cause many harmful health consequences, but one of their most severe actions is carcinogenesis. Plenty of information exists about the literature website, PubMed, on different health consequences triggered by heavy metals. However, this knowledge has not been incorporated, which necessitates the incorporation of this analysis. We describe how people are exposed to heavy metals and the forms the metal properties impact to various processes.

Aluminum

Many separate pathways of exposure cause aluminum exposure. Exposure to aluminum has been reported in poultry, vaccinations, and in aluminum salts used in manufacturing processes and consumer goods. Certain goods that include aluminum salts include some antacids and antiperspirants. Aluminum has been closely associated to cancer in the breast tissue. Mice subjected to the same type of aluminum salt exposed to antiperspirants develop breast cancerous cells. Related effects were found in tests of human breast cell cultures [1-3]. It is also speculated that heavy metals have a role in sarcomas [4].

The study showed that chronic sensitivity to aluminum comprising heavy metal salts may cause a neuroectodermal tumor atypical. There are many ways why aluminum can cause cancer. After exposing cells to this factor, one research has reported reduced expression of the tumor suppressor gene BRCA1 and DNA maintenance genes. More human breast cells display an improved growth capacity when subjected to aluminum [4].

Aluminum was found to function as a metalloestrogen, breast cancer develops from over stimulation of estrogen. Thus, antiestrogen medication should be used. Similar carcinomas analyzed in another region of the body revealed elevated amounts of aluminum and other heavy metals [5].

This study suggested that manganese would prevent malignant growth in the bladder. Chelation therapy has been presented as the cure of aluminum toxicity. In addition, aluminum bioaccumulates in soft and skeletal tissues, which are priority organs for extracting aluminum from the body [6].

Chemotherapies are usually obtained by patients. This compound may be used to reduce aluminum concentration in the body. Owing to the toxicity of Betamethasone, its use has several dangerous side effects. Several interesting alternatives to deferoxamine have been discovered, but none are as successful as deferoxamine. The easiest approach to minimize the effects of aluminum is to limit sensitivity to the product. The other way to reduce public awareness is the usage of reverse osmosis filtration. This technique has been demonstrated to have a strong ability to remove vast quantities of aluminum from a copper mining waste [7].

Arsenic

Arsenic is a harmful, carcinogenic factor that may cause cancer. Often, arsenic might come from making food or consuming polluted water. Sometimes, arsenic comes from occupational exposure to arsenic-based pesticides. As well as industrial pollution [8-11].

Exposure to heavy metals such as arsenic arises through interaction with the atmosphere, especially the natural arsenic in soil. This heavy metal has been detected in many malignant growths. Several studies show that arsenic increases risk of lung, bladder and skin cancer. E-cigarettes have been linked to mortality from diseases including the colon, stomach, kidneys, lungs, and nasal passage. Epidemiological reports have shown that arsenic exposure may raise the risks of pancreatic and non-lymphoma Hodgkin's throughout the future [12-15].

Heavy metals cause adverse health consequences by producing elevated amounts of free radicals and oxidative stress. The cancer induced by arsenic as a consequence of epigenetic alterations of DNA, histones, and miRNA. One study shows that copper can induce unwanted growth cycles in macrophages as well as lung epithelial cells [16].

It was observed that ROS originating from arsenic stimulated macrophages in M2 process which suggests lung carcinogenesis. From the rat experiments, a special mechanism of action was shown in humans. This heavy metal was shown to down regulate p53, the removed inhibitor contributed to a reduced product of p21. Any "cancer-like cells" somehow activated the cell-signaling process that triggers carcinogenesis [17].

It was observed that arsenic decreased intracellular concentrations of glutathione, a natural antioxidant. There is fear that the cell might be prone to oxidative stress [18]. There is another alleged carcinogenic impact which traces to DNA regulation. DNA beta- polymerase is active in this repair mechanism, and arsenic prevents its function at high concentrations [19].

A new biological pathway behind inducing tumor development was observed in human bladder cells. Chronic arsenic exposure can induce genetic alterations, which can influence cellular function. The most recommended method to combat arsenic is by chelators. BAL (anti-lewisite) may be used as chelator for metal ions [20, 21].

Dimercaptopropane-1-sulphonate (DMPS) was prescribed as a remedy for arsenic toxicity as a prevention for it. It was a positive with no side effects, which shows the value of potential testing. Antioxidants can help decrease arsenic damage when someone is exposed to it. Developing innovative techniques to avoid disclosure is important. Apple, rice and fruit juices are highly popular exposure sources. Recommended are 5µg/L arsenic amounts in apple juice, owing to its widespread consumption by adolescents [22, 23].

Rice is being genetically engineered to avoid arsenic absorption. The atmosphere is being taken over by bacteria that are vying for arsenic. The usage of sprinkler irrigation has the ability to decrease arsenic levels in rice by precipitating arsenic from the rice [24, 25].

Beryllium

Beryllium is significant in technology and industries. The major source of beryllium emissions is from power plants when they disperse it into the environment. Airborne inhalation is suspected of being the source of lung cancer, and is also a subject of several clinical trials [27-28].

The two different beryllium studies have also led to its more important roles as a lung cancer risk factor. In comparison, elevated toxicity amounts to beryllium triggered increased incidence of lung cancer. The usage of beryllium in the dental industry causes workplace toxicity hazards [29-30].

The researchers determined that wearing safety clothing decreases the amount of exposure for humans. Elevated beryllium concentrations were found in patients with stage III breast cancer. However, some heavy metals were found, so there is no obvious position for them at this stage. The future occurrence of osteosarcomas is also a possibility from beryllium toxicity [31, 32].

There are minimal findings on the carcinogenic pathways of beryllium. The majority of the latest literature is on lung disease. Another unhealthy mechanism observed by researchers was that e-cigarettes may induce a higher level of pro-inflammatory cytokines produced from leukocytes in the lung. Any of these proteins may have an impact on the inflammatory mechanism [33, 34].

Beryllium can often affect inappropriate genetic alterations.

Estrone, the estrogen hormone, was found to inactivate the p16 gene, a recognized tumor suppressor gene. Chelators are medications used to extract beryllium from the body and reduce its adverse consequences [36]. Chemicals include penicillamine (DPA) and tiron which are effective on livestock [37].

Mice were handled with meso2,3-dimercaptosuccinic acid (DMSA) to rescue an infant suffering from heavy metal toxicity. This finding offers clear proof that merits further study. There has been considerable initiative to minimize workplace sensitivity to this metal [38]. These initiatives include organization systems implemented to test blood samples for beryllium sensitization during jobs, supplying rest to the workplace, and enforcing equipment controls [39]. Attention was also paid to teaching staff regarding the value of safety devices and the possible dangers of prolonged beryllium toxicity [40].

Cadmium

Cadmium is a particularly hazardous metal, and thus an industrial contaminant [41]. Cadmium pollution occurs from pollutants from numerous sectors that use cadmium, including processing, metal research, and avoiding precipitation of pigments [42]. Soil pollution is primarily through inhalation, smoking and ingestion of waste water and food. Another cause of pollution is the ground on which it is known to have cadmium above the safety levels in certain situations [43].

Environmental contamination from consumption to metal in the environment has been noted [44]. Cadmium has been associated with a wide variety of various forms of cancer [45]. Cadmium is likely related to gallbladder cancer. The medical experts are studying the molecular formula of gallstones from cancer patients. Higher amounts of cadmium, along with other toxic heavy metals were found by researchers [46]. While cadmium did not cause the symptoms, it may be related to carcinogenic growth of the bladder [47].

Cadmium has been found to be carcinogenic in cells in a laboratory environment. Increased cadmium levels were also observed in brain tumors, indicating a possible role in carcinogenesis in the brain [48]. Studies also shown that the reaction to cadmium may cause cancer in the pancreas [49]. This metal has been implicated of the development of both leukemia and lymphoma. The patients with these forms of leukemia revealed considerably more amounts of cadmium in their blood and lower levels of magnesium in their bodies [50].

Investigations into cadmium amounts in the urine found that it raised likelihood of contracting gastrointestinal cancer [51]. The pathways of cadmium that lead to carcinogenicity are oxidative stress, DNA methylation, inhibition of DNA repair, and apoptosis. Chronic and acute sensitivity to cadmium results in shifts in gene regulation, which is correlated with elevated risk of cancer. Primary proteins showed unregulated expression like DNAJB9 involved in cell destruction and metallothioneins [52, 53]. Many proteins were down regulated as well, including those that control transcription. There are no standard preventive procedures for the management of cadmium toxicity. However, there is continuing study on reducing the harmful consequences of this metal [54]. Cadmium selective peptoids have been shown to be effective in decreasing cadmium absorption. It has been observed that most plants produce compounds named “flavonoids” that have antioxidant properties [55].

Additional research is advised to decide how the composition of [L]- α-lactone-cadmium influence its behavior. There have been studies into the usage of stem cells to treat the symptoms of cadmium toxicity (56). The testes of rats were harmed by elevated levels of cadmium. Bone marrow mesenchymal stem cells treat the testes to show more acceptable amounts of proteins linked to apoptosis control. Cell remodeling in testes was an outstanding indication of damage recovery following spermatozoa damage [57].

Lead

Lead is a harmful heavy metal that may causes health issues [58]. One form that waste reaches the human food chain is from polluted produce. Lead is also found in industrial aircraft liquids. It has been determined that this polluting substance contributes large amounts of lead. Higher blood lead levels were found in smokers relative to nonsmokers. Some jobs often subject workers to lead, such as logging [59].

Epidemiological trials have been undertaken to assess whether lead toxicity raises cancer incidence. Further proof reveals that there is no causal impact of lead on the chance of developing cancer [60]. Lead and cadmium were detected in significant numbers in glioma patients, suggesting that these two compounds can cause adverse effects. The higher the lead intake, the more likely an individual would develop kidney cancer [61].

A separate study identified a correlation between elevated blood lead levels and a higher risk of kidney cancer. The lead is one of the major elements of heavy metals in gallstones. This may well be the precursor to carcinoma of the gallbladder. In their study, it was noticed that sensitivity to lead raises the likelihood of lung, head, and larynx cancer [62].

Although toxic elements such as lead are found at higher amounts in the pancreatic tissue of certain people, the development of this condition remains a mystery. The literature has not identified carcinogenic pathways of lead; however, possible mechanisms have been suggested. Lead tends to interrupt the tumor-suppressor pathway by disabling tumor-suppressor genes, triggering mutations in the DNA repair mechanism, and disturbing cellular repair and DNA [63].

There is support for lead playing a part in inducing oxidative stress and modifying chromosomal function and pattern. Lead has shown that it may inhibit the translation process by replacing zinc in certain proteins that regulate transcription. Serum calcium has a lower chance of developing renal cell carcinoma that suggested the need for a clinical trial to determine the relevance [60].

Therapy with chelation is the preferred medication for people with lead poisoning. There are numerous chelators that are being used to avoid anemia and other disorders correlated with lead, such as tin malignancy in humans. There is study into the effects of less harmful treatments. Garlic in patients with non-severe lead poisoning has been shown to reduce serum lead levels, and it alleviates symptoms. The most effective approach to minimize blood lead is to eliminate toxicity [64].

The Environmental Protection Agency could also collaborate with business to minimize lead pollution and employee exposure. It has been proposed that detection of lead pollution sites, accompanied by elimination or avoidance, is the best way to minimize exposure to this heavy metal [62].

Mercury

Mercury can cause health problems because of its toxicity. Mercury is an element occurring in small quantities in the soil and in certain rocks, most current due to human caused contamination. Mercury has a broad variety of applications, all of which end in toxicity. Many causes of lead have been reported, including fossil fuel pollution, dental accidents, some batteries, and burning medical waste [65, 66].

Compounds such as mercury may be vaporized in soil and water sources and penetrates the atmosphere. Eating vast amounts of fish can be a key cause of ambient mercury contamination. The mechanism by which mercury is penetrating the environment has not been discovered, but it is bio-accumulating in shellfish and tuna [67, 68].

A potential causal function was not established but exposure to renal cancer may be involved, since this organ is a mercury candidate. Increased mercury exposure has been related to many forms of cancer, notably those of the liver and gastrointestinal tract. Mercury was found in statistically higher amounts in gallstones in patients with gallbladder disease [69].

A causal link was not found, but a role in carcinogenic production was suspected. Like any of the other heavy metals, mercury has the ability to cause malignant development by many unique pathways. The diseases have the capacity to create free radicals and damage DNA structure and maintenance [70].

However, these studies show that mercury can influence genetic stability through methylation that may in turn impact health. It is possible that mercury decreases glutathione levels in the body, which increases the carcinogenicity of mercury. This would also increase susceptibility to oxidation of cellular materials. Chronic oxidative stress may cause lipid peroxidation contributing to carcinogenesis [71, 74].

In this way, mercury will alter microtubules and disrupt cell division. Chelation therapy is a popular method for extracting mercury from the body. Dimercaptosuccinic acid (DMSA) and dimercaptopropane sulfonate (DMPS) are the most powerful chelators in a clinical setting. Efficacy trials have been conducted to investigate unproven chelators for mercury. Drugs like deferasirox and deferiprone have been studied in rodents. It was shown that this mixture was able to reduce the impact of mercury [75, 77]. One special experimental chelator was thiol-modified nanoporous silica. At low amounts, this substance is poisonous and, in situ, emits mercury, cadmium, arsenic, antimony, thallium, lead, and chromium [78].

Nickel

Heavy metals such as nickel have attracted interest owing to their potential to serve as carcinogens [79]. Exposure may cause toxic effects in an atmosphere or occupational setting. Exposure to nickel may come from many industries like refining, metal alloys and electroplating. The migration of mercury from water to fish and other animals of the food chain pose a danger to humans [80].

Soil contamination will be another potential source of the poisonous metal. Oil refining emissions have been targeted as a potential cause of nickel emissions [81]. Many different forms of cancer are linked with nickel toxicity [82]. There is a substantial correlation between the incidence of cancer in lung and sinus tissues and toxicity of smoke. High levels of serum nickel in patients with breast cancer were statistically significant in another study suggesting probable carcinogenic effects [83].

The prevalence of acute myeloid and lymphoblastic leukemia is related to heavy metal exposure. Elevated quantities of nickel and 8- hydroxy-2'-deoxyguanosine were observed in kids who have leukemia. These results suggest that nickel can trigger oxidative damage. Studies have also shown that nickel amounts are elevated in patients with pancreatic cancer. When contemplating the existence of nickel, data leads to potential carcinogenic results [84].

A recent research connects persistent allergic stimulus from many heavy metals to the growth of cutaneous T-cell lymphoma. Furthermore, the reported association between radiation and liver cancer mortality rates. Nickel has several cancer inducing pathways. E-cigarettes activate an epigenetic pathway that influences particular long noncoding RNAs. The gene 3 (mEG3) was shown to downregulate through deacetylation and methylation of the related promoter. This process has been shown to inhibit PHLPP1 gene output and upright the hypoxia-inducible factor-1α gene [85].

Nickel has been shown to generate free radicals that contributes to cancer, i.e. it is related to the carcinogenic phase. The sensitivity of rats to this hard metal often affects microRNA (miRNA) transcription control status [78]. These transcripts also have functions in immunity and inflammation that have all indicated cancer function [86].

Analysis looked at the function of nickel in chronic inflammation. Increased sensitivity to SQSTM1 and TNF proteins that act to regulate inflammatory levels and induced carcinogenesis. Heavy metals may induce epigenetic modifications; such as changes in DNA methylation, e.g. nickel ions were found to induce the tri-methylation of histone H3K4 [87].

Vaporized nickel is associated with improper transcriptional activation, suggesting another carcinogenic pathway. Compared to other heavy metals, nickel could have had a distinct reaction. Sodium diethyldithiocarbamate is a strong chelator of nickel carbonyl, but there is not any data to say it is toxic to nickel cancer [88]. Researchers also researched chelation with an aim of eliminating nickel from the atmosphere. It has been reported that EDTA caused the nickel in Arundo donax L from contaminated soils [89].

Nickel hydroxide is suitable for systems; which nickel amounts are unsafe. It was observed that CaNa [2] EDTA recovers brain damage from nickel chloride, and eliminates nickel from Cirrhinus mrigala [90].

Radium

Radioactive particles can adversely impact health. The poisonous gas comes from the decay of the radium into toxic radon. Occupational and natural radium are vulnerable to radiation ionizing [91]. The coal mining sector is a major area for risks and hazards [92].

Wastewater is polluted with toxic waste from mining as well. Radium contamination results in more health issues from dirt, construction products and water supplies. Research in Italy states the radon gas accumulates in places such as basements and closets [93]. It was observed that radon binds to cigarette smoke which led to higher radon levels in the house. It indicates that smoking is an occupational contaminant of radium. Radium is a recognized carcinogen that induces cancer. Radiation exposure can cause lung cancer, because lung cancer and radiation exposure both develop when the same cells are over-stimulated [94].

The radioactive existence of this metal should not involve chelators. It was determined to have many special implementations. Patients suffering from ankylosing spondylitis have the right to take radium. It was determined that injection of this metal raises the likelihood of some types of leukemia. Injecting mice with radium culminated in the production of osteosarcomas. In a separate scenario, there was a

cutaneous squamous cell carcinoma in response to therapy for infected material. Patients that have extravasated toxic chemicals may have supervision by a dermatologist [95].

Conclusion

Heavy metals have an important effect on human wellbeing, and cancer growth. The accessible study has highlighted many areas of focus for potential studies. An educated understanding of carcinogenic pathways is needed. Which could help create targeted interventions for particular heavy metals. Consolidation is another aspect to remember in going on. Successful awareness initiatives must be introduced in regions that have elevated levels of heavy metal emissions.

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