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Lead Associated Nephrotoxicity: A Global Concern.

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ABSTRACT

Amongst toxic heavy metals, lead ranks as one of the most serious environmental poisons all over the world. An occupational and environmental exposure to lead remains a serious problem in many developing and industrializing countries, as well as in some developed countries. Lead exposure can be detrimental to every organ in the human body with kidney and brain being predominantly susceptible to its deleterious effects. An association between lead poisoning and renal diseases in humans has been recognized and documented by several studies. Excessive exposure to lead may cause acute or chronic nephrotoxic effects. Studies suggest that prolonged lead exposure may be an overlooked risk factor for chronic kidney disease. Majority of lead associated renal toxicity are a result of the previous chronic exposure, ongoing chronic exposure or current high acute exposure to lead. Both glomerular and tubular effects have been reported. Glomerular effects range from high molecular weight proteinuria to a nephritic syndrome whereas tubular changes consist of an enhanced urinary excretion of enzymes. Lead poisoning and associated nephrotoxicity is an important and preventable health problem that remains to be fully addressed. However due to lack of education regarding the dangers of working with lead or lead containing products, potential health hazards of lead poisoning still exist and are rising in India. The regulatory bodies should be more vigilant and make it mandatory to evaluate and create awareness among the workers as well as general population about the lead toxicity and should insist on regular health checkups to prevent adverse health effects.

Keywords: Blood lead level, Moonshine whisky, Nephropathy, Plumbism.

INTRODUCTION

Lead, a ubiquitous and versatile metal has been used by mankind for over 6000 years and is one of the most widely scattered toxic metals in the environment today.[1] Although lead is a useful metal in various industries and is being utilized in lead acid battery manufacturing, lead bullets, painting, plumbing, printing, lead mining and refining, smelting and many other useful industrial activities but it serves no useful function in human body and is quite toxic for humans.[2-4] Exposure to lead is widely recognized as a major risk factor for several human diseases but the structure of industrial ecological systems has made exposure to lead unavoidable. Lead enters into the body either by ingestion, inhalation or by dermal contact (organic lead). Once absorbed, around 99% of lead is retained in the blood for nearly 30-35 days and is subsequently disseminated and accumulated in various tissues viz kidneys, brain, liver, aorta, lungs, spleen and bones.[5] Lead is chemically very similar to calcium and once in the body, is handled as if it were calcium.[6] Exposure to lead causes variety of deleterious effects in almost all the organs and organ systems of the body among which nephrotoxic, neurobehavioral, hematological, reproductive and cardiovascular effects are predominant.[1,7-10]

Human exposure to lead and uptake of this non-essential element have consequently increased, more so dramatically in the past 50 years due to its increased use in industrial processes and products.[11] Both environmental and occupational lead exposure continues to pose major public health problem in the exposed population of many developing and industrializing countries. Excessive exposure to lead may cause acute or chronic nephrotoxic effects. Studies suggest that prolonged lead exposure may be an overlooked risk factor for chronic kidney disease.[6] First description of kidney disease and interstitial nephritis in a lead poisoned artist was given by Lancereaux.[12] But it was not until the late

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1920s when an epidemic of chronic nephritis in Queensland, Australia was linked to childhood lead poisoning and the full spectrum of lead induced nephropathy was revealed.[13] A chronic lead nephropathy remarkably similar to the Queensland variety was described from United States (US) among the individuals consuming lead contaminated illegally distilled moonshine whisky.[14]

Sources of lead exposure

Human exposure to lead is from many sources like air, food, dust, soil and water. Certain products like lead soldered cans, traditional folk remedies, cosmetics, artisan ceramics and environmental emissions containing lead are some common sources of lead exposure.[15] Lead is also found in several industrial sources, which cause occupational lead exposure. Chief among these are accumulator battery industry, lead smelters, lead or silver ore mining, lead refining and lead based paints. Returning servicemen with retained bullets or shrapnel and employees or participants in indoor firing ranges also have significant lead exposure.[6]

Environmental exposure

Prior to being unleaded, combustion of leaded petroleum was a significant contributor to lead toxicity.[16] There was a substantial increase in the environmental lead contamination due to the use of leaded petrol and the increased community exposure to it.[15] However lead was removed gradually from the gasoline or petrol in most of the developed countries. Blood lead levels (BLLs) in the general population in those countries who use unleaded petrol or gasoline have fallen dramatically over the past few decades.[6]

Lead based paints can be a major source of lead poisoning, especially among children. The painted surfaces of old houses can serve as potential reservoir of lead. Direct ingestion of lead paint, lead contaminated house dust and water has been identified as a major contributor to lead poisoning among children. Studies have shown that lead contaminated dust or drinking water are the major determinants of blood lead concentrations.[7] Children are more susceptible to the effects of environmental lead than adults because of increased gastro intestinal absorption of lead in children as they can absorb lead 5-10 times more efficiently than adults. Moreover their exploratory behavior and frequent hand to mouth activity causes increased intake of lead in children and makes them more vulnerable to lead toxicity.[15] As children are under rapid developmental phase, the effects of lead toxicity are more impounding in them.

Lead pipes may have been used in older distribution systems and plumbing. From the drinking water perspective, the universal use of lead compounds in plumbing fittings and as solder in water distribution system is important. Lead is present in tap water primarily from plumbing systems in which the pipes, solder fittings or service connections to homes contain lead. Polyvinyl chloride (PVC) pipes also contain lead compounds leaching of which can result in high lead concentration in drinking water.[17] According to Indian standard drinking water specification 1991, highest desirable limit of lead in drinking water is 0.05ppm with no relaxation for maximum permissible limit.[17] Leaching of lead from cooking and storage vessels containing lead, into water and from lead containing cooking vessels with acidic food conditions contribute to the potential lead exposure through ingestion. Moreover in India, elevated lead concentration in beer (10mg/l) and the use of arsenate pesticides can also contribute to lead exposure through ingestion route.[18]

Skin products containing lead such as litharge deodorant or kohl eye shadow can also render a person lead intoxicated by sufficient absorption through skin.[19,20] Some traditional medicine practices like Ayurvedic, Chinese, Middle Eastern and Hispanic cultures have been found to use lead in their medicinal preparations and can cause lead toxicity.[21] For e.g. Ayurvedic medicines like Jambrulin, Guglu, Gulkand, Chandraprabhavati etc. are used for treating various diseases and have been found to cause lead toxicity.[22-24]

Occupational exposure

Occupational exposure to lead is one of the important sources of lead toxicity. Among adults, exposure is usually greatest for those who come into closest contact with lead in production process or who work with lead.[4] Major occupations associated with lead toxicity are battery makers, brass workers, lead smelters, gunshot makers, jewelers, painters, pottery workers, solderers, pipe cutters and people working with lead mining and lead casting.[15] In developed countries strict control and improvement strategies have helped to ensure the minimal occupational exposure to lead but problem still persists in developing countries. In many countries small scale business (repairing automobile radiators, artisans, pottery and ceramic ware production), often a home based occupation are carried out in unregulated workshops, in close proximity to the locality and the lead fumes or dust generated pose an exceptional health hazard to children and adults living nearby.[15] Those who are exposed to this heavy metal for many years get the lead deposited in soft tissues and bones making these organs endogenous sources of lead for many years even when they are removed from the ongoing exposure.[4] According to United States Occupational Safety and Health Administration (OSHA) regulation (29 CFR 1910.1025 App B), workers with single BLL of ≥60µg/dl or an average of the last three BLLs or all BLLs over the previous six months at ≥50µg/dl must be removed from his or her regular job to a place of significantly lower exposure. In

children the generally accepted blood lead value, which signifies a potential hazard, is 10µg/dl. However the lower limit of BLL below which no toxicity is observed, has not been established.[6]

Many of the individuals working in lead mines or industries are unaware of the effects related to lead poisoning and work without using personal protective equipments (masks, gloves, safety glasses) even though they are provided.[25] Most of them belong to socioeconomically poor class and once affected are recommended to remain away from the work place, but due to economic constrain, lack of employment opportunities, social conditions and desire to work with the same job only, they do not follow the advice which further exposes them to this toxic metal.[4,25]

Lead associated nephropathy

An association between lead poisoning and renal diseases in humans has been recognized and documented by several studies.[26-28] In the early 20th century there were several reports of progressive renal failure due to occupational exposure to lead.[6] Several epidemiological studies conducted worldwide found a direct correlation of impaired renal function tests (serum creatinine, blood urea nitrogen, creatinine clearance, urea clearance, glomerular filtration rate, β2-microglobulin clearance, urinary albumin) with the length of lead exposure.[6,29] Lead toxicity can cause varying degrees of diffused interstitial or peritubular fibrosis.[6] Studies have shown an association between BLLs and blood pressure, with hypertension being a cardinal feature of lead associated nephropathy.[28,30,31]

Excessive exposure to lead can cause acute or chronic nephrotoxic effects. Two types of nephropathy, acute and chronic nephropathy has been observed in humans.[32] In acute nephropathy both morphological and functional changes are seen in kidney. Morphologically the tubular epithelium shows the degenerative changes and the nuclear inclusion bodies containing lead protein complexes. Functionally there is generalized deficit of tubular transport mechanisms (Fanconi syndrome).[32] The effects of acute nephropathy are usually reversible with chelation therapy. Chronic lead nephropathy is an irreversible renal disease that develops over months or years of excessive exposure to lead.[33,34] Chronic occupational exposure to lead has been linked to high incidence of renal dysfunction characterized by glomerular and tubulointerstitial changes resulting in chronic renal failure, hyperuricemia, and hypertension. Chronic nephropathy occurs as a progressive tubulointerstitial nephritis, which is difficult to diagnose at early stage. Also there is increased urinary excretion of low molecular weight proteins and lysosomal enzymes.[35] The gross pathological finding is of a granular contracted kidney. The tests evaluating the glomerular filtration rate (creatinine clearance, blood urea nitrogen, serum creatinine) can be used to detect the renal effect caused by occupational exposure to lead. But, by the time these tests turn abnormal, nephropathy has already reached the irreversible phase that leads to renal insufficiency.[33] Chronic lead nephropathy has been reported previously in adults who had ingested leaded paint during childhood and those who consumed illicitly distilled alcohol (moonshine whisky).[13,14]

Majority of lead associated renal toxicity are a result of the previous chronic exposure, ongoing chronic exposure or current high acute exposure to lead. Both glomerular and tubular effects have been reported. Glomerular effects range from high molecular weight proteinuria to a nephritic syndrome whereas tubular changes consist of an enhanced urinary excretion of enzymes.[30,33]

Indian perspective

In most of the developed countries, concerted efforts have led to a reduction in the incidence of plumbism. However it still continues to be a significant public health problem in many developing countries like India where the sources of exposure are multifaceted. In India >80% of used lead is recycled by unorganized sectors who barely comply with government regulations. Most of them being small family owned smelting industries are not registered and are hardly visited by regulating authorities. Limited awareness, poor personal hygiene and work place ethics among workers in such industries has resulted in high BLLs.[4] Lead is also commonly incorporated in kohl (ancient cosmetic from Middle East), litharge deodorants, nail paints, sindoor (traditional cosmetic item used by married Indian ladies), and in various Ayurvedic preparations which serve as a significant potential source of lead exposure.[19-24]

The potential health hazards of lead poisoning still exist and are rising in India, due to lack of education regarding the dangers of working with lead or lead containing products. The regulatory bodies should be more vigilant and make it mandatory to evaluate and create awareness among the workers as well as general population about the lead toxicity and should insist on regular health checkups to prevent adverse health effects.

CONCLUSION

Exposure to environmental and occupational lead is clearly a major public health hazard of global dimensions. Data and experimental evidence clearly points to potential nephrotoxicity and progressive renal failure from exposure to lead. Developing countries like India have increased ambient levels of lead and the additional occupational exposures, nutritional deficiencies (iron, protein) and various infections can potentiate the overall impact of lead

on human health. Lead poisoning and associated nephrotoxicity is an important and preventable health problem that remains to be fully addressed. It is therefore essential to implement national as well as international policies related to tackle this problem. Research and regulatory bodies should provide unique exposure information to scientists, physicians and health officials to help prevent diseases due to various environmental chemicals/metals like lead. Moreover recognition and inclusion of heavy metal assays as diagnostic guide will definitely improve patient management. Screening, monitoring, intervention and evaluation are critical for development of rational cost effective and science based public health policies aimed at achieving these goals.

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