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Impact of Heavy Metal Exposure on Women and Human Reproductive Health

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***Abstract*:** Quality of the environment plays a significant role in human health. It was estimated that one-quarter of the global disease burden and more than one-third of the burden among children was due to modifiable environmental factors. The group of heavy metals represents pollutants that are concerned with serious health problems connected with a high global annual emission rate. The toxic effects of the heavy metals are often expressed differently on the outcome of human reproduction. Recommended medical surveillance for all heavy metals requires emergency departmental care. Literature study explored that there is a gap of knowledge in the proper toxicity survey.

Introduction

A recent report by the World health Organization (WHO) confirms that quality of the environment plays a significant role in human health. It was estimated that one-quarter of the global disease burden and more than one-third of the burden among children was due to modifiable environmental factors (Prüss-Üstün and Corvalán 2006). On one hand, healthier environments can help in the prevention of a wide range of disorders and decrease the morbidity rate among humans. On the other hand growth of the human population forces a higher demand for food, consumption, and industrial products, and consequently, leads inter alia to increasing environmental contamination. The group of heavy metals represents pollutants that are concerned with serious health problems connected with a high global annual emission rate. These elements are not only resistant to decomposition in natural conditions, but may also bioaccumulate and biomagnify in the food chains. However, 'heavy metals' is imprecise term which is widely used in the scientific literature. It is commonly defined as a group of elements with a specific density of more than 5 g/cm^3 (Duffus 2002). It is also generally accepted that some of these metals are essential for living organisms in small quantities, but toxic in higher concentrations or in other speciation forms, e.g. copper (Cu), chromium (Cr), manganese (Mn) and zinc (Zn), while other are not considered to have any specific metabolic role and are generally classified as obligatory toxic, e.g. cadmium (Cd), mercury (Hg) and lead (Pb). Arsenic (As), although chemically classified as a metalloid, is also often included in the heavy metals group. These elements are natural constituents of the earth's crust and it is beyond any doubt that indiscriminate human activities have drastically altered their geochemical cycles and biochemical balance. The main global sources of anthropogenic contamination by heavy metals include different branches of industry, the power industry, transport, municipal waste management, waste dumping sites, fertilizers and waste used to fertilize soil (Szyczewski et al., 2009). Exposure to such heavy metals poses a serious health hazard primarily because the effects of such exposure are not felt immediate, rather it manifests after

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many years of exposure. An overwhelming amount of scientific data has now been accumulated on the toxicity of these heavy metals (Cooksey, 2012, Chen et al., 2012).). It appears that heavy metals can be involved in alterations of gene expression and lead to associated epigenetic changes.

A large number of studies have been done on hose metals that are biochemically essential as well as those which have no known role in the normal functioning of the human body, but are considered to be toxic. Many such elements also bear significance from the point of environmental pollution and contamination (Lauwerys, 1975; Pier, 1975). The importance of such studies assumed more importance when the biochemical roles of such elements became clear. Almost all the metals, including those regarded to be highly toxic, have been observed to readily bind to the metabolically essential mercapto groups. Both in vitro and in vivo studies have reported that toxic metals can replace essential metals in many of their metalloenzymes, with resultant changes in activity. Metals are also observed to bind to proteins, phospholipids and nucleic acids, and have been shown to effect a change in the conformation of enzymes required for normal functions, or to uncouple oxidative phosphorylation (Wada et al., 1977). Although there are adequate instances that portray health risks to both adults and children when exposed to these metals, Bushnell and Jaeger (1986) has documented several instances where economic and societal pressures have resulted in the continued use of materials that are potentially toxic, hazardous and injurious to public health.

Studies have suggested that environmental influence play an important role in determining health status of individuals. For example, the state of Punjab has been reported as having a high degree of water pollution due to heavy metal from untreated industrial effluent discharge and high pesticide usage in agriculture. These exposures are directly associated with potential risk factors for adverse reproductive and child health outcome (Thakur et al., 2010). Kumar (2004) also reported that harmful effects of occupational exposure on the reproductive system and releted outcomes have gradually accumulated in recent decades.

Effect of Toxic Elements on Women

Interestingly, most of the earlier studies on metal toxicity on humans had focused upon male individuals as the subject of study. The toxic effects of the heavy metals are often expressed differently among women. With the initiation of studies on the effects of environmental pollutants among females, there is increasing evidence of effects at specific periods in a woman's life, even though the amount of information is scanty. An important example is the *Itai-Itai* disease, which is a combination of osteoporosis, osteomalacia and renal damage caused by consumption of cadmium-polluted rice. Women may be at greater risk than men, because of their increased gastrointestinal uptake of cadmium at low iron stores. This is common among women of childbearing age. An improvement of iron status has a positive effect on cadmium exposure in the sense that its absorption decreases. Cadmium accumulates in the kidney with a half-life of 10 years to 30 years. The health effects appear around menopause, concurrent with the peak in renal cadmium concentrations. With regards to lead, about 90per cent of body lead is localized in the bone. Bone lead reflects long-term exposure and proves valuable in epidemiologic studies. There is a significant release of bone lead after the menopause, in association with the acceleration of bone resorption. As a result, postmenopausal women may be at increased risk of adverse effects of lead. Data on the effect of other toxic metals is extremely limited among women. To fully understand the significance of bone as a target tissue of lead toxicity, as well as a reservoir of systemic lead, it is necessary to define the effects of lead on the cellular components of bone. Skeletal development and the regulation of skeletal mass are ultimately determined by the four different types of cells. These are osteoblasts, lining cells, osteoclasts and osteocytes. These cells line and penetrate the mineralized matrix, and are responsible for matrix formation, mineralization, and bone resorption. They remain under the control of systemic and local factors. Systemic components of regulation are the parathyroid hormone, 1, 25-dihydroxyvitamin D3, and calcitonin, while numerous cytokines and growth factors are the local regulators. The toxic elements can directly or indirectly alter bone cell function through changes in the circulating levels of the hormones that modulate bone cell function. They may also impair the ability of cells to synthesize or secrete other components of the bone matrix, such as collagen or bone sialoproteins (osteopontin). In many instances, the element may directly substitute for calcium in the active sites of the calcium messenger system, resulting in loss of physiological regulation.

Effects of Toxic Elements on Human Reproductive Health

Infertility has been already recognized by the World Health Organization as a considerable public health issue worldwide and has become a serious medical challenge. It is believed that approximately 15per cent – 30per cent of couples are diagnosed with unexplained infertility (Vayena et al, 2001). It is beyond any doubt that lifestyle and quality of the ambient environment can play a fundamental role in human reproductive success (Sharpe and Franks .2002). Below it is demonstrated that exposures to heavy metals such as Cd, Pb or Hg may be highly involved in impaired human fertility.

Another important area is the effect of the heavy metals on the outcome of human reproduction (Wirth and Mijal, 2010). While experimental animal and human occupational studies with high exposure levels generally support an adverse role for these toxic metals in human reproductive outcomes, information on the effects of low, environmentally-realistic exposure levels of these metals on male reproductive outcomes is limited. Epidemiological evidence has strongly indicated that exposure to the toxic elements can lead to impairments in reproductive outcome. These may be in the ability to conceive, spontaneous abortions and miscarriages, pre-term births, low birth weight, birth defects and perinatal mortality. Another important issue here is declining fecundity. Many of the heavy elements are the principal factors that have the potential to affect the stages of male and female reproduction. There are very few studies examining the effects of exposure to low levels of these metals on male reproductive health.

It is believed that metals may affect the male reproductive system directly, when they target specific reproductive organs, or indirectly, when they act on the neuroendocrine system. These effects can be long lasting and irreversible if Sertoli cells are disrupted during fetal development. Metals can affect the testis size, semen quality, the secretory function of the prostate and seminal vesicles, the reproductive endocrine function and can lead to the loss of fertility and impotence (Wirth and Mijal, 2010; Apostoli and Catalani, 2011). When toxic metals accumulate in the epididymis, prostate, vesicular seminalis or seminal fluid, they have the potential to cause impairment in progressive sperm motility (Hess, 1998). In addition, metals can cause hormonal imbalance by affecting the neuroendocrine system, thereby disrupting the secretion of androgens from Leydig cells or Inhibin B from Sertoli cells (Jensen et al., 2006). There is also growing evidence that oxidative stress is implicated in the pathogenesis of male infertility and that human spermatozoa are particularly vulnerable to oxidative stress (Garrido et al., 2004; Makker and Agarwal, 2009). The effects on the male reproductive system also include erectile dysfunction, asthenospermia, hypospermia, teratospermia, changes in sperm count and sperm motility. The females are affected with failure to conceive and reproductive wastage. Studies on the effects of exposure on the age at menarche and reproductive wastage among women are also limited in number. These observations clearly suggest that Hg may have a significant impact on human reproduction, especially for some occupational groups or populations with prevalence of aquatic food in the diet (especially in Asia). There is a need to understand the mechanisms behind the Hg-induced impairment of fertility, and the complete ecotoxicological risk assessment requires further and complex investigations while the aquatic food – strict quality advisories. It was demonstrated that smoking can be a significant source of heavy metals especially Cd and Pb. Globally, 1 billion men and 250 million women smoke every day. In 2011, over 30per cent of Poles smoked cigarettes regularly (Bednarski et al. 2007/2008). It was estimated that 100,000 children in Poland are born annually by mothers who smoked during pregnancy. It is forecasted that between 2000 – 2025, the number of cigarette-smoking women will increase by 8per cent (Fronczak et al, 2012). On the other hand, Dechanet et al. found that cigarette smoking among women can lead to implantation failure and higher risk of miscarriage (Dechanet et al., 2011). Another problem is the preterm delivery, stillbirth and the smaller weight of the newborn, as well as the future health problems of those children (bronchopulmonary dysplasia, upper and lower respiratory infections, asthma), (Been et al., 2013). A recent systematic data review found an association between maternal smoking and reduced cognitive abilities later in the life of child Clifford 2012. Klejewski et al. (2012) also found that tobacco smoking, both active and passive, affects pregnant women and can lead to preterm delivery, stillbirth and a lower weight of the newborn. These, in turn, can be followed by health issues during early childhood. On the other hand, it was a surprising fact that non-smokers more often had a miscarriage in their medical history than other groups. Several investigations have highlighted the potential impact of tobacco smoking on the occurrence of some gynaecological disorders. Jabłonowska et al. examined tobacco smoking, HPV (human papillomavirus) infections, and changes in the cervix, and their results revealed a direct relationship between cigarette smoking, HPV infection and significant increase of high grade squamous intraepithelial lesion (HSIL) in histological images. Cerqueira E. et al., examining the cytogenetic effects of cigarette smoking on exfoliated cells from the uterine cervix in women with normal smears, and women with inflammatory atypia, squamous intraepithelial lesion (SIL) (cervical intraepithelial neoplasia, CIN 1–3) and cervical cancer, confirmed these results (Jabłonowska 2012, Cerqueira 1998). On the other hand, according to Yuping Zhou et al., exposure to cigarette smoke may provide a protective effect in case of endometrial disease among smokers. They revealed that *in vivo*, mice exposed to cigarette smoke similarly showed increased expression of HOXA10 (homeobox A10) and PGR (progesterone receptor) in the endometrium. HOXA10 and PGR drive endometrial differentiation, and both are suppressed in endometrial tumours and in endometriosis. Another aspect is the impact of smoking on semen. Studies have produced different results. The relationship between smoking and semen analysis parameters (morphology, motility and concentration) has been confirmed, but the mechanism is still not completely understood (Taszarek 2005, Davar et al., 2012, Mitra et al., 2012,). Mitra et al. revealed that lower sperm motility ($P < 0.001$) and increased sperm morphological defects ($P < 0.0001$) were associated with smoking habits (Mitra et al., 2012).

Heavy metal poisoning is the accumulation of heavy metals, in toxic amount, in the soft tissues of the body. Symptoms and physical findings associated with heavy metal poisoning vary according to the metal accumulated. Many of the heavy metals, such as Zinc, Copper, Chromiium, Iron and Manganese, are essential to body function in very small amounts. But, if these metals accumulate in the body in concentrations sufficient to cause poisoning, then serious damage may occur. The heavy metals most commonly associated with poisoning of human are lead, mercury, arsenic and cadmium. Heavy metal poisoning may occur as a result of industrial exposure, air or water pollution, foods, medicines, improperly coated food containers, or the ingestion of lead-based paints.

Research conducted in recent years has increased public health concern about the toxicity of lead at low dose and has supported a reappraisal of levels of lead exposure that may be safely tolerated in the workplace. Kosnett et al., 2007 has reported that certain appears as part of mini-monograph on adult lead exposure, we summarize a body of published literature that establish the potential for hypertension, effects on renal function, cognitive dysfunction, and adverse female reproductive outcome in adults with whole-blood lead concentration <40 microg/DL. Based on this literature, and the collective experience in evaluating lead-exposed adult, research recommended that individuals be removed from occupational lead exposure if a single blood lead concentration exceeds 30 microg/DL or if two successive blood lead concentrations measured over a 4-week interval are > or = 20 microg/dL.

Cure and Prevention

Recommended medical surveillance for all heavy metals require, emergency departmental care. One of the important therapies as explained by Kosnett et al., (2007) is decontamination. This denotes a kind of treatment removal of the patient from the source of exposure so as to limit the dose. Resuscitation a good supportive care is critical mechanical ventilation and organ dysfunction. Chelation is also rarely indicated in the emergent setting. A possible exception is lead encephalopathy. Consideration of chelation therapy for patients with suspected or confirmed metal exposures should be made in conjunction with a medical toxicologist or the local poison control center. The most recent Centers for Disease Control (CDC) guidelines recommend routine screening of children for lead exposure. The CDC recommends close lead-level monitoring of children with lead levels greater then 10 micrograms/dL.

Conclusion

Increasing urbanization and industrialization can lead to the elevated risk of human exposure to heavy metals, and consequently, health implications including disturbances in reproduction. It is therefore important to continue the investigations on metal-induced mechanisms of fertility impairment on the genetic, epigenetic and biochemical level. Simultaneously, parallel epidemiological data are necessary to assess the real risk of exposure for each population, and the participation of heavy metals in unexplained fertility problems. Analytical data on the accumulation of metals in gynaecological organs and tissues can also provide interesting information, particularly if correlated with the quality of the environment, lifestyle and diet. The above findings from different scientific studies also indicated that the degree of toxic manifestation of different metals depends on dose, duration, route of administration and other physiological factors specially nutrition. The sign and symptoms of metal toxicity depend on the duration of exposure, type of metal, condition of workplace, socio-economic status and history of disease. But extensive literature study explored that there is a gap of knowledge in the proper toxicity survey. Thus, further efforts should be made to widen our knowledge in this unmapped area of research.

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