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A Review on the Impact of Heavy Metals on Female Fertility

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ABSTRACT

In human health status, the quality of the environment plays an important role. With increased demand for industrial products, food, consumption by continuous growth of human population leads to excessive environmental contamination. The heavy metal group represents pollutants and in natural conditions these elements are not only decompose resistant but may also bio-magnify and bio-accumulate in the food chains which concerns with health problems, seriously connected with a annual emission rate globally. Environment exposure to the most comprehensively distributed pollutants like Cd, Pb, Hg and their contamination causes the main health hazards and at the same time heavy metals exhibits a high level of toxicity against living organisms. According to the considerable toxicological study report from the recent decades, the heavy metals adverse effect on human beings as immunodeficiency, kidney & other organ failures, neurotoxicity, osteoporosis as well as latent involvement in impaired fertility. Epidemiologically and clinically, it is difficult to interpret the metal-induced effect on female reproduction as other factors are also involved. Toxic manifestations depend on intensity of exposure, timing and duration. The eco-toxicological and risk evaluation needs further critical investigation. Along with the implementation of law regulations for the emission limits, the development of awareness campaigns are also required to decrease the harmful habits & lifestyle to develop the successful techniques for fertility protection.

Introduction

In human health status, the quality of the environment plays an important role [1]. With increased demand for industrial products, food, consumption by continuous growth of human population leads to excessive environmental contamination. The heavy metal group represents pollutants and in natural conditions, these elements are not only decompose resistant but may also bio-magnify and bio-accumulate in the food chains which concerns with health problems [2,3].

Effluence of the heavy metals into the environment can happen through various processes or pathways which includes the air, surface water and the soil. Air is affected by the methods like combustion, extraction and processing where as the surface water is affected through the direct deposition, runoff into the water resources, and emission from the storage & transport [4]. Greater exposure of humans mainly via contaminated food & water consumption or via contaminated air inhalation (or tobacco smoke) [5,6]. Consequences of metals on the reproductive system of females can emerge from their activity. Within the various stages, this begins in the fetal life, during the early stages of the development. It can include subfertility, infertility, growth retardation with the intrauterine region, unforced abortions, distortions, congenital abnormalities, post natal mortality, learning and behavioral impairments & early ageing are the indicators representing the abnormal female reproductive functioning.

In 35-40% pregnancies with in humans, the pregnancy loss (abortion) is the end point for identifying the functioning of the female reproductive system. This can lead to early loss of pregnancy and can also include a large proportion of genetic or chromosomal deficits. Environmental factors have been linked to some and later abortions are clinically manifested in remaining 10-15% [7]. Thus, in humans there seems to be fetal loss remarkably in high rate. Other factors such as hormonal imbalance, age, genetics, behavior, sexually transmitted diseases or male fertility factors, ovarian reserve may affect the outcome and difficult to interpret the metal-induced effects on female reproduction epidemiologically & clinically. Moreover, in checking out reproductive adverse effects, intensity of exposure, timing and duration are important [8]. When metals interact occupationally or environmentally with certain reproductive target organs the effect may be direct or indirect (when metals act on other systems or endocrine system). The metals for an extended period

of time susceptibly damage the ova and ovaries directly.

Due to metal exposure increased risk of miscarriage, placental insufficiency, fetal malformation & premature birth are suggested by some experimental studies [9]. Warning signals from the current evidence shows the vulnerability of female reproductive system to toxic agents and the exposure of working women potentially to metals are increasing day by day globally [10].

Metals as Endocrine-Disrupting Chemicals & Female Reproduction

The consequences of occupational or environmental exposure of metals & use of synthetic estrogen demonstrated the altered reproductive function in females like early menopause & decreased fertility by the ability of endocrine-disrupting chemicals (EDCs)[11,12].

The female fetus is an easy target to environmentally induced reproductive abnormalities, the synthetic hormones sensitizes the gonadal organogenesis and after exposure until decennary there is no visibility of reproductive disease by the EDCs research in animals & humans by the lessons learned from many years[13].

Chemical exposure during the time of developmental periods results in hormone signaling disturbances and could come up with decline in human population conception rates and ovarian disorders [14]. There is a confirmation that EDCs are contributing to increased rates of polycystic ovarian syndrome, aneuploidy, altered cyclicity, premature ovarian failure and fecundity but, the mechanisms by which these chemicals alter follicle development are not fully concluded [15-17]. In humans, the individuals who are exposed to pesticides and metals are reported with altered cyclicity. In fact, women have been well known with cycle irregularities in whose mothers were exposed to EDC in utero [18].

In 25-50% of females, leiomyomas or uterine fibroids are the most usual tumor occurring in the female reproductive system. During premenopausal years, the risk of uterine fibroids development increases with age but with the start of menopause tumors typically revert [19,20]. The uterine fibroids in humans by EDCs is less clear [21].

Effects of Cadmium (Cd), Lead (Pb) & Mercury (Hg) on the Female Reproduction System

Environment exposure to the most comprehensively distributed pollutants like Cd, Pb, Hg and their contamination causes the main health hazards and at the same time heavy metals exhibit a high level of toxicity against living organisms. According to the considerable toxicological study report from the recent decades, the heavy metals adverse effect on human beings as immunodeficiency, kidney & other organ failures, neurotoxicity, osteoporosis as well as latent involvement in impaired fertility [22,23]. Based on the epidemiological acute metal poisoning data the long-term exposures to low concentrations relates the actual health concern & which can probably affect the human population in large part [24].

The World Health Organization already recognized infertility as a significant public health issue worldwide and has become a consequential medical challenge [25]. It is believed that unexplained fertility has been diagnosed in 15-30% of couples approximately [26]. Uncertainly for the human reproductive success the quality of atmospheric environment & life style plays a basic role [27].

Cadmium (Cd)

In 20th century, the release of Cd and its compounds well used in disparate industrial branches have been increased dangerously. Now-a-days, cigarette smoking is appraised as a vital source of cadmium exposure. The inauspicious health effects of cadmium may takes place at lower levels than previously foreseen has also been suggested. In the human body the bones & kidneys are the first targets of cadmium [28]. To the cadmium action the reproductive system also seems to be vulnerable in the human body. Females with smoking history are demonstrated with accumulation & increased levels of Cd in the human endometrial tissue [29]. Cadmium is contemplated as a metalloestrogen. It can join & stimulate the oestrogen receptors (α and β) as demonstrated & at the same time progesterone receptors upregulation can also be done. Cadmium thus linked as a probable causative negotiator of oestrogen-dependent diseases, such as endometriosis, endometrial & breast cancer & spontaneous abortions [30-32]. Furthermore, cadmium leads to the conversion in the mRNA expression in human endometrial

endothelial cells which is responsible to increase in the number of angiogenic molecules PLGF (placentation growth factor) and VEGF-A(vascular endothelial growth factor). It was also found that by the existence of endometrial stomal cells, this occurrence is altered and that Cd on cadherin dependent cell-cell junctions can have an indirect adverse effect.

Expression of PLGF & VEGF-A mRNA influences the angiogenesis processes in endometrial cells which play important role in the implantation, placentation, embryogenesis. These disorders cause implantation failure, subfertility, endometrial dysfunction, premature delivery, preeclampsia & spontaneous abortions [33].

Lead (Pb)

Lead is another heavy metal extremely emitted worldwide. Roughly equal proportions of general population are exposed to lead from the food and air. Mainly due to emission of Pb from petrol into the atmospheric air give rise to significant pollution, during the last century [34]. Pb is still well used in industrial branches although there is dramatical decrease of lead in petrol over the last decades.

The concentration of lead in the human body is dependent on a number of factors in which age, place of residence & lifestyle play a pivotal role. Individuals who abused alcohol & smoking and who live in industrialized areas were found with raised levels of lead in human endometrium was demonstrated [35]. The level of lead increases with number of years was also found which perhaps related with the release of lead earlier accumulated in bones. As demonstrated by some studies that lead even at low doses could be very harmful, despite there is no clear confirmation that it can act on reproduction system at such levels. This requires more, complex studies however, which cannot be ruled out.

Some surveys have suggested that Pb through its possible teratogenic action can straightly leads to a higher threat of spontaneous abortions [36,37]. The well calculated adverse effect of lead on the placental vascular disorders inducement or the human sperm quality are the unintended causes behind this judgment [38]. It was also noticed that Pb from bone stores increase with mobilization by the pregnancy-related metabolic changes & cause the fetus for exposure to the endogenous metal content. Therefore, it is postulated that intake of calcium during the second half of pregnancy may decrease lead mobilization and interestingly calcium play a defensive role against this process according to the reports [39].

Mercury (Hg)

The activities of the humans especially burning & mining of the coal lead to the mobilization of mercury and the levels in air, soil, fresh & ocean water have been raised. The main reason for higher release of the mercury has been observed since 1800, which can be due to “Industrial Revolution” [40]. In the food chain due to Hg biomagnifications & bioaccumulations the food gets contaminated & consumption of contaminated food is the major source of exposure, in particular with aquatic invertebrates & fish being a main source of exposure to methyl mercury. Individuals operating or having contiguity with dental amalgam (a mercury alloy with different metals worn for dental fillings) are the special group to concern [41].

The latent effect of Hg on human reproduction is still little known, regardless of the common neurotoxicity by mercury compounds [42]. Based on the 6 epidemiological studies observed within the Europe, women who have been exposed to mercury due to occupational reason are identified with abnormalities of the menstrual periods which includes the changes in bleeding pattern causing amenorrhea or dysmenorrhea and the length of the menstrual cycle is also affected [43]. If the women were exposed to the mercury in the term of pregnancy which can affect the maternal blood, hair of the infant and can also be related to birth weight of the new born. Based on the above observations the levels of mercury can show greater impact on the reproduction within the human population, specifically in the occupational groups or the population feeding on the aquatic food [44].

Conclusion

With the increased industrialization and consumption of contaminated food & water or by inhalation of contaminated air, the heavy metals show various adverse effects on female reproduction in several stages. The loss of pregnancies can be the end point by monitoring the effects. Epidemiologically and clinically it is difficult to interpret the metal-induced

effect on female reproduction as other factors are also involved. Toxic manifestations depend on intensity of exposure, timing and duration. The eco-toxicological and risk evaluation needs further critical investigation. Along with the implementation of law regulations for the emission limits, the development of awareness campaigns are also required to decrease the harmful habits & lifestyle to develop the successful techniques for fertility protection.

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