The effect of chronic lead exposure on fertility in female rats via hypothalamic – pituitary and ovarian axis

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Abstract
Lead is a ubiquitous environmental pollutants, known to impede the reproductive function. However, mechanism through the adverse effects are mediated, has not been clearly elucidated. In order to get insight into the mechanism, the effect of lead on fertility impairment in female rats via hypothalamus-pituitary-ovarian axis were examined. Chronic exposure to lead (5mg/kg body weight of lead acetate was given subcutaneously every second day from the age of 16 days until the age of 71 days), FSH and estradiol-17β level of blood while LH and progesterone level revealed variable effects. Degranulation and degeneration of few gonadotrophs of pituitary, reversible ovarian vascular damage with haemorrhages, follicular degeneration and necrosis, suppressed puberty growth rates, delayed vaginal opening and disrupted estrus cycling were other adverse effects induced by chronic lead exposure.

Keywords: Lead, Toxicity, Hypothalamus, Pituitary, Ovary, Hormones

Introduction
Lead poisoning was considered primarily as occupational disease adult as major public health problem (Lin-Fu, 1992) [9]. Reproductive toxicity associated with lead exposure have been noticed since classical time (Bell and Thomas, 1980) [2]. A number of recent studies have demonstrated the effect of low level lead exposure on growth and development (Schwartz, 1992) [10]. Lead induced reproductive toxicity in adult male rats is well documented. The effects described include altered circulating level of testosterone and Leutenizing hormone in the plasma and pituitary (Bell and Thomas, 1980) [2] and described LH-binding sight and decreased sperm counts in the testes (Sokol et al. 1985; Sokol and Berman, 1991) [11, 12]. However, little is known regarding the lead induced toxicity on female reproduction. Correlation between maternal blood –lead levels during pregnancy and premature delivery, stillbirths and reduced birth rate have been described by Mc. Michael et al. 1986 [13] and Bornschein et al., 1987 [3].

The hypothalamic-pituitary-gonadal axis function in a closely regulating manner to produce the concentration of circulating sex steroids required for the development of sexual physiology and maintenance of sexual behavior. The interplay of hormones in the HPG axis may be affected at any level from hypothalamic secretion of tropic releasing to direct effect on gonadal metabolism of sex steroid. It has been suggested that in adult male lead act both at both at the level of hypothalamic-pituitary unit and directly at gonadal sites to disrupt reproductive physiology and behavior. The aim of the present study was to examine the effect of chronic lead exposure on fertility impairments in female rats via hypothalamic – pituitary-ovarian axis.

Materials and Methods
Female Wistar rats were selected for this study. They were maintained under standard laboratory condition (12hrs.light, temperature 22±2°C) and given food and water ad libitum, out of two groups of female rats (each containing 10 rat), 5mg/Kg weight of lead acetate was given subcutaneously to the first group every second day from the age of 16 days until the age of 71 days and second group of female rats served as a control receiving 5mg/kg body weight sodium acetate simultaneously. Age of vaginal opening assessed in female animal and estrus cycle was monitored by daily analysis of vaginal smear at the age of 71 days. At euthanisation rats were decapitated and blood was collected for analysis of FSH, LH, Progesterone and estradiol-17β. Assays of these hormones were carried out in endocrinology laboratory of C.C.S University Meerut.
National Institute of Immunology, New Delhi. FSH and LH level in serum of Animals of both group determined by radioimmunoassay as described by Badger et al., 1983 [1]. Serum estradiol -17β and progesterone were determined using specific kits.

Results
In this study, the rats of both group appeared healthy and showed no significant changes in food intake, growth rate or body weight however lead exposure regulated in significantly delayed vaginal opening and disruption in estrous cycling in 60% of the experimental animal. As revealed from data given Table no 1, chronic lead exposure with 5mg per kg body weight on alternates days from the age of 16 days to the age of 71 days produced significant decrease in the level of 17β-estradiol and FSH while progesterone level revealed no significant alteration in the blood of female rats level of LH showed slight elevation.

Table 1: Effect of lead exposure on serum progesterone, 17β estradiol, LH and FSH in female rats.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Progesterone</th>
<th>17β estradiol</th>
<th>FSH</th>
<th>LH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>819.4± 82.6</td>
<td>50.6± 4.2</td>
<td>0.61±0.04</td>
<td>0.54±0.03</td>
</tr>
<tr>
<td>treated</td>
<td>828.1± 63.8</td>
<td>36.3±2.9</td>
<td>0.43±0.06</td>
<td>0.59±0.07</td>
</tr>
</tbody>
</table>

Data as mean± S.E.pg/ml
a. Data as mean ± S.E.ng/ml
b. Significant at < 0.005

Discussion
The present study was designed to examine the effect of chronic lead exposure on the reproductive potential of female rats. Schwartz et al., 1986 has demonstrated growth deficits in lead exposed children, however no significant change in growth rate and body weight was reported in the female rats exposed to lead in this study. The delay in vaginal opening which we have observed in female rats, following lead exposure is consistent with similar findings reported by Grant et al., 1976 [8] and Kimmel et al. Complete disruption of estrous cycling due to lead exposure was reported by Martin et al., 1996 while in this study only 60% of rats were showed disrupted estrous cycling.

Under the influence of FSH and LH, secreted from the gonadotrophs of pituitary, whose master control lies in the hypothalamus in the form of GnRH ovaries secrete 17β estradiol and progesterone. In this way hypothalamus – pituitary-ovarian axis play important role in fertility capabilities of mammalian species. Reproductive toxins adversely affect the function of this action axis and have been responsible for the impairment in the fertility. In this study chronic lead exposure produced adverse effect on the level of 17β estradiol, FSH and LH. Most environmental pollutant, including heavy metals, have been shown rats.to effect ovarian steroidogenesis.

Our results reveal that lead interferes at several sites in the steroids biosynthesis via Hypothalamus-pituitary –gonadal axis and affects ovarian morphology, which leads to impairment of fertility in female

References