The Changes in Sex Hormones in Female Working in Batteries Manufacturing Plant

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Abstract

Lead has toxic effects on reproduction of both male and female. It can cause decreased sex drive, infertility and abnormal menstrual cycle in women. This study was designed to evaluate the effect of exposure to lead in batteries female workers on sex hormones level in the serum. Thirty nine (39) female workers (volunteers) in Iraqi Batteries Manufacturing Plants, Al-Waziriya / Baghdad were participated in this study. They are classified into 3 groups, first group included fourteen (14) female that have been employed for 1-7 years, second group included thirteen (13) female that have been employed for 8-14 years, third group included twelve (12) female have been employed for 15-22 years and fourteen females were included as the control. Blood lead level, serum FSH, LH, prolactin and total testosterone were measured and compared for all subjects. The results indicated that mean of blood lead levels (BLL), testosterone levels were highly significant in all worker groups compared to the control (p<0.005). Prolactin levels in group I and FSH in group III were significantly higher than that in control (P<0.005) and (P<0.05) respectively. LH levels in groups II and III were significantly higher than that in control (P<0.05, P<0.005 respectively). High incidence of hirsutism (48%) and miscarriages (50%) were observed in worker groups compared to control (11%). The results indicated that there are hormonal changes in female workers exposed to lead associated with increased incidence of hirsutism and miscarriages compared to non exposed females.

Key words: Lead , Sex hormones hyperandrogenemia

الخلاصة

تسعية وثلاثون امرأة عاملة في معمل صناعة البطاريات في بغداد شاركت في هذه الدراسة كمتطوعات قسمت العاملات إلى ثلاث مجموعات اعتمادا على فترة التعرض للرصاص.

1- المجموعة الأولى تشمل (9) عاملة وفترة الخدمة تتراوح بين (18-27) سنوات وعمر (18-54) سنة.
2- المجموعة الثانية تشمل (13) عاملة وفترة الخدمة تتراوح بين (16-48) سنة وعمر (20-51) سنة.
3- المجموعة الثالثة تشمل (17) عاملة وفترة الخدمة تتراوح بين (22-51) سنة وعمر (24-62) سنة.
4- المجموعة الرابعة: مجموعة السيطرة وتشمل (14) امرأة بوسط عمر (18-29) سنة.

وجد في هذه الدراسة أن هناك تغير في مستويات الهرمونات الجنسية عند النساء العاملات عند مقارنتها بمجموعة السيطرة. وجد كذلك أن مستويات الهرمونات اللويني في المصل يزداد عند العاملات اللواتي تعرضن للرصاص لفترة طويلة. أما هورمون محفز الحصى في المصل فزاد أولئك الذين تعرضوا لفترة طويلة وأما هورمون البيبلاكتين فين زاد فقط بعد التعرض لفترة قصيرة للرصاص. وكذلك هورمون التستوستيرون الكلي يزداد عند النساء العاملات متصلاً مع زيادة في نسبة الشعرانية والانسقاط عند العاملات مقارنة بمجموعة السيطرة.

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Introduction
Some scientists cautioned the Romans of the danger of inhaled fumes from lead smelting (9). With the industrial revolution, lead poisoning became a common occupational problem. The reproductive effects of lead poisoning were also noted by the turn of the century and many articles describe the high rate of stillbirths, infertility and abortions among women in the pottery industry, or who were married to pottery workers (2).

The most important route of absorption in occupational setting is through inhalation of lead dust and fumes. In addition, workers may eat, drink or smoke in lead-dust-contaminated areas resulting in some ingestion as well. Storage battery manufacture involves considerable exposure to lead oxide dust, in addition to fumes from welding of battery connector (9).

Lead can cause decreased sex drive and infertility in women. In addition, it can cause abnormal menstrual cycles (dysmenorrhea, menorrhagia and amenorrhea), premature birth, spontaneous miscarriages, and stillbirths. The incidence of polymenorrhea, prolonged and abnormal menstruations, hypermenorrhea was significantly higher in the lead exposed group (female workers of lead battery plants) than in controls (4). This study was designed to evaluate the hormonal changes (LH, FSH, prolactin and testosterone) in women whom exposed to lead in batteries manufacturing plants through inhalation and direct contact with active constituent of batteries.

Subjects and Methods
This study was carried out on female workers employed in Iraqi batteries manufacturing plants, Babylon 1 and 2 in Al-Waziriya / Baghdad for the period of three months from January to April of 2005.

Thirty nine (39) female workers were participated in this study, they work 6 hours per day every other day and had been employed for at least 1 year in the plant.

The subjects were classified into 3 groups according to the duration of exposure to lead (employment in the plant) as follow:
Group I includes fourteen (14) female that have been employed for 1-7 years with range age (24-50) years (29.2±7.2) years.
Group II, includes thirteen (13) female that have been employed for 8-14 years with range age (30-55) years (37.9±7.9) years.
Group III includes twelve (12) female that have been employed for 15-22 years with range (32-52) years (41.1±6) years.

Fourteen healthy women, not exposed previously to lead with age range (24-50) years (29±7.1) were utilized as control.

Individual questioner protocol was followed for all women concerned with gynecological and obstetrical history including married or not, age of marriage, number of children, type of delivery (normal or caesarean section), number of miscarriages, growth of their infants, if they work during pregnancy, regular or irregular menstrual cycles, if they have amenorrhea, dysmenorrhea or menorrhagia. Appropriate day for each female (between 2nd and 5th day of menstrual cycle) was selected to consider follicle phase for FSH and LH assay, and female were advised to fast 12 hr. before sampling, for appropriate analysis of prolactin. Blood samples (14 ml) were drawn from each patient and control by vein puncture left to clot and serum was separated by centrifugation.

Blood lead levels were measured using the slotted quartz tube method (9). LH, FSH and prolactin levels in serum were analyzed using radioimmunoassay methods (9) while testosterone was assessed according to the method of Abraham et al (9). All these kits supplied by Immunotech, A Beckman coulter company (France).

Independent t-test was used to examine the difference in the mean of control and workers, also the differences among worker groups themselves. P-values < 0.05 were considered as significantly different. Pearson correlation (r) was performed to find relationship between exposure time and testosterone levels.

Results
Table (1) shows the ages and occupational (exposure) periods of female worker. The number of married were 3,6,7 in I, II, III groups respectively. The mean age of control group was 29.1±7.1 years and the number of married was 5.

Table (2) shows mean blood lead levels in all groups of workers are significantly (p<0.005) higher than that of the control group. Groups II and III workers have significantly higher blood lead levels than that of group I workers (p<0.05). Serum total testosterone levels in all three worker groups were significantly higher in comparison with that of the control group (P<0.005). Total testosterone level for group I workers was the highest one. However group I workers have a serum total testosterone level that was significantly higher than that of groups II and III workers (P<0.05). Mean prolactin level in group I workers shows highly significant increase compared to that of the control group (P<0.005).While mean prolactin levels in groups II and III were non-significantly elevated compared with the control group (P>0.05). Group I workers have prolactin levels.
Sex Hormones Changes

Mean FSH level of workers group I and II were non-significantly elevated (P>0.05) compared to control group. While mean FSH levels of workers group III workers was significantly elevated (P<0.05) in comparison with that of the control group. LH levels show non significant difference among worker groups themselves. Mean LH level in group II workers was elevated significantly in comparison with that of the control group. LH levels show non significant difference among worker groups themselves. Mean LH level in group III workers was significantly elevated (P<0.05) in comparison with that of the control group. A negative correlation was found between time of lead exposure and serum testosterone levels (r=-0.43, P<0.05). In table (3) all workers groups have percentage of hirsutism (17.9%) and miscarriages (50%) higher than that in control group. In table (3) all workers groups have percentage of hirsutism (17.9%) and miscarriages (50%) higher than that in control group.

### Table 1: Demographic data of workers and control women

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age (mean ±SD) (years)</th>
<th>Occupation period (mean ±SD) (years)</th>
<th>Number of married</th>
<th>Number of unmarried</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>29.2±7.2</td>
<td>3.6±1.9</td>
<td>3</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>II</td>
<td>37.9±7.9</td>
<td>11.1±4.4</td>
<td>6</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>III</td>
<td>41±6</td>
<td>18.2±2.8</td>
<td>7</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Control</td>
<td>29.1±7.1</td>
<td>-</td>
<td>9</td>
<td>5</td>
<td>14</td>
</tr>
</tbody>
</table>

### Table 2: Serum levels of lead, testosterone, prolactin, follicle stimulating hormone (FSH) and luteinizing hormone (LH) in females working in battery industries

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead (µg/dl)</td>
<td>13.4±4.5</td>
<td>21.4±6.7** a</td>
<td>31.6±7.7** b</td>
<td>29.7±7.3** b</td>
</tr>
<tr>
<td>Testosterone (ng/ml)</td>
<td>0.156±0.5</td>
<td>0.458±0.15**a</td>
<td>0.356±0.13**b</td>
<td>0.28±0.1** b</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>8.5±4.1</td>
<td>19.7±11.9** a</td>
<td>10.7±7.2** b</td>
<td>11.7±8.1** b</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>6.9±2.7</td>
<td>13.3±14.7** a</td>
<td>10.9±8.4**a</td>
<td>14.4±13.6* a</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>8.8±3.3</td>
<td>11.1±3.7** a</td>
<td>14.7±10.4* a</td>
<td>17.3±9.1** a</td>
</tr>
<tr>
<td>LH/FSH</td>
<td>1.2±1.64</td>
<td>0.83±0.45**a</td>
<td>1.3±1.3** a</td>
<td>1.2±0.85** a</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD
*P<0.05 significant difference from control group
**P<0.005 highly significant difference from control group

Values with different letters (a,b) are significantly different (P<0.05).

### Table 3: Distribution of female workers with hirsutism and miscarriages

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I No. (%)</th>
<th>Group II No. (%)</th>
<th>Group III No. (%)</th>
<th>Total</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hirsutism</td>
<td>2(14)</td>
<td>2(15)</td>
<td>3(25)</td>
<td>7(17.9)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Miscarriages*</td>
<td>1(33)</td>
<td>3(50)</td>
<td>4(57)</td>
<td>8(50)</td>
<td>1(11)</td>
</tr>
</tbody>
</table>
Discussion
The results indicated that mean of blood lead levels (BLL) were significantly higher in all worker groups compare to the control group (p<0.005), this may be due to long term exposure to lead oxide which used in batteries manufacturing plant. The workers practice in improper environment, they were not wearing face mask, cloves with bad ventilation inside plant rooms, in addition to that workers were eating inside the manufacturing rooms, which means they did not follow the conditions of occupational safety. The workers in group I had blood lead levels significantly lower than that in groups II and III (P<0.05); this may be due to longer exposure time in groups II and III than that for group I.

It has been reported that patients with blood lead levels less than 45µg/dl do not require chelation therapy (10). The mean blood lead levels in most female workers are less than that reported in previous studies (11,12), because females in present study are working every other day in the plant since 1.5 years, because of shortage of labor raw materials. The mean serum testosterone levels in all worker groups were significantly higher than that of control group (P<0.005)(table 2). This elevation in serum testosterone levels in worker groups may be attributed to that lead affects dopaminergic control of prolactin secretion from pituitary gland, according to previous study on rats (16).

The results demonstrated that only group III workers have mean serum FSH level significantly higher than that of the control group (P<0.05) (table 2). The elevation in serum FSH also reported by Ng et al. (17) where significantly higher serum FSH and LH levels were observed in lead-battery male workers, during less than 10 years exposure period, whereas those exposed for 10 years or more showed normal serum LH and FSH concentrations. However, Vivoli G et al. (18) reported negative relationships between blood lead level and LH and FSH in males with lead levels higher than 9µg/dl.

Group I workers are presented with serum LH not significantly different from that in control group (P>0.05) while group II and III have mean serum LH significantly higher than that in control group (P<0.05,P<0.005 respectively) (table 2). This elevation in serum LH levels are in agreement with that reported by Rodamalans et al (19) who reported that in lead-smelter workers, serum LH levels are significantly raised, as compared with controls.

more than 1 week exhibited a significant increase in Gonadotropin releasing hormone (GnRH) mRNA, but with attenuation of the increase at higher concentrations of lead with increased duration of exposure. They concluded that the signals within and between the hypothalamus and pituitary gland appear to be disrupted by long-term lead exposure.

LH stimulates theca cells of ovary to produce testosterone in female (14). However, in this study, it has been found that as LH level increases, testosterone level decreases (table 2), indicating that elevation of testosterone level in female workers may be extra ovarian. However most of studies concerning lead were applied on animal models so it is difficult to compare present findings with their results. Group I have a high mean prolactin levels which are significantly higher than that of control group (P<0.005); while mean prolactin levels in group II and group III were not significantly different from control group (P>0.05) (table 2). Prolactin release from the pituitary is under tonic inhibitory control from hypothalamus-derived dopamine or prolactin inhibitory factor (PIF). Thyrotropin-releasing hormone (TRH) in turn is stimulatory to prolactin release. Estrogen can directly sensitize the pituitary to release prolactin (15). The elevation of prolactin levels in worker groups could be attributed to that lead affects dopaminergic control of prolactin secretion from pituitary gland, according to previous study on rats (16).

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Furthermore, Yen (20) suggested that basal LH levels are elevated in women who are exposed to lead, compared to women with low lead exposure. This suggests that the exposure to lead may be associated with an increase in LH levels. An increase in LH levels may result in an increase in LH mRNA expression in the hypothalamus, which could lead to an increase in hypothalamic GnRH expression and subsequently an increase in pituitary LH synthesis (5). This increase in LH synthesis may contribute to the observed increase in LH levels in women exposed to lead.

In this study, we found that LH levels were increased in female workers in the battery plant compared to control workers. This increase in LH levels was associated with a decrease in FSH levels, which may be indicative of a decrease in FSH production. The increase in LH levels may be due to an increase in LH mRNA expression in the hypothalamus, which could lead to an increase in GnRH expression and subsequently an increase in pituitary LH synthesis (5). This increase in LH synthesis may contribute to the observed increase in LH levels in women exposed to lead. Although the mechanism behind the increase in LH levels is not fully understood, it is possible that the increase in LH levels is due to a decrease in FSH levels, which may be caused by a decrease in FSH production. This decrease in FSH levels may be due to a decrease in FSH mRNA expression in the hypothalamus, which could lead to a decrease in GnRH expression and subsequently a decrease in pituitary FSH synthesis (5). This decrease in FSH synthesis may contribute to the observed decrease in FSH levels in women exposed to lead. However, further research is needed to fully understand the mechanisms behind the increase in LH levels and decrease in FSH levels in women exposed to lead.

References