

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

Mohammed A. Taher ^{*1}, Salim A.Hammadi^{**}, Ali A.Ali^{**}

^{*1}Department Clinical Laboratory Sciences, College Of pharmacy ,university of Baghdad, Baghdad-Iraq.

^{**} Department Clinical Pharmacy, College Of pharmacy ,university of Baghdad, Baghdad-Iraq

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 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

تسعة وثلاثون امرأة عاملة في معمل صناعة البطاريات في بغداد شاركن في هذه الدراسة كمتطوعات قسمت العائلات الى ثلاث مجاميع اعتمادا على فترة التعرض للرصاص.

١- المجموعة الأولى تشمل (١٤) عاملة وفترة الخدمة تتراوح بين (٧-١) سنوات ويعمر (٥٠-٢٤) سنة.

٢- المجموعة الثانية تشمل (١٣) عاملة وفترة الخدمة تتراوح بين (٨-٤) سنة ويعمر (٣٠-٥٥) سنة.

٣- المجموعة الثالثة تشمل (١٢) عاملة وفترة الخدمة تتراوح بين (١٥-٢٢) سنة ويعمر (٣٢-٥٢) سنة.

٤- المجموعة الرابعة: مجموعة السيطرة وتشمل (١٤) امرأة بمتوسط عمر (٢٩±٧) سنة.

وجد في هذه الدراسة ان هنالك تغير في مستوى الهرمونات الجنسية عند النساء العاملات عند مقارنتها بمجموعة السيطرة. وجد كذلك ان مستوى الهورمون اللوتيني في المصل يزداد عند العاملات اللواتي تعرضن للرصاص لفترة طويلة اما هورمون محفز الجريب في المصل يزداد فقط عند التعرض لفترة طويلة. اما هورمون (البرولاكتين) فيزداد فقط بعد التعرض لفترة قصيرة للرصاص. كذلك هورمون التستوستيرون الكلي يزداد عند النساء العاملات متصاحبا مع زيادة في نسبة الشعرانية والاسقاطات عند العاملات مقارنة بمجموعة السيطرة.

¹corresponding author email Mohammed – Taher 43 @yahoo.com

Received 21-11-2005

Accepted 7-10-2006

Introduction

Some scientists cautioned the Romans of the danger of inhaled fumes from lead smelting⁽¹⁾ 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⁽³⁾.

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 are with 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.⁽⁵⁾ LH ,FSH and prolactin levels in serum were analyzed using radioimmunoassay methods^(6,7,8) 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

significantly higher than that of groups II and III of workers ($P < 0.05$). Mean FSH level of group III workers was significantly elevated ($p < 0.05$) in comparison with that of the control group. While mean FSH levels of workers group I and II were non-significantly elevated ($P > 0.05$) compared to control group. FSH levels show non significant difference among worker groups themselves. Mean LH level in group II workers was elevated significantly in compared to that of the control group. LH level in group III workers shows a highly

significant increase compared with control group ($P < 0.005$). Furthermore mean LH level in group I workers was non-significantly elevated ($P > 0.05$) compared to that of the control group. LH levels show non significant ($P > 0.05$) difference among worker groups themselves. There are non significant differences among LH/FSH ratio in all three groups of workers and control group ($P > 0.05$). Also LH/FSH ratio show non significant ($P > 0.05$) difference among worker groups.

Table(1) Demographic data of workers and control women.

Groups	Age (mean \pm SD) (years)	Occupation period (mean \pm SD) (years)	Number of married	Number of unmarried	Total
I	29.2 \pm 7.2	3.6 \pm 1.9	3	11	14
II	37.9 \pm 7.9	11.1 \pm 1.4	6	7	13
III	41 \pm 6	18.2 \pm 2.8	7	5	12
Control	29.1 \pm 7.1	-	9	5	14

Table (2) Serum levels of lead, testosterone, prolactin, follicle stimulating hormone (FSH) leutinizing hormone (LH) in females working in battery industries.

Parameters	Control	Group I	Group II	Group III
Lead (μ g/dl)	13.4 \pm 4.5	21.4 \pm 6.7** a	31.6 \pm 7** b	29.7 \pm 7.3** b
Testosterone (ng/ml)	0.156 \pm 0.5	0.458 \pm 0.15**a	0.356 \pm 0.13**b	0.28 \pm 0.1** b
Prolactin (ng/ml)	8.5 \pm 4.1	19.7 \pm 11.9** a	10.7 \pm 7.2 ^{NS} b	11.7 \pm 8.1 ^{NS} b
FSH (mIU/ml)	6.9 \pm 2.7	13.3 \pm 14.8 ^{NS} a	10.9 \pm 8.4 ^{NS} a	14.4 \pm 13.6* a
LH (mIU/ml)	8.8 \pm 3.3	11.1 \pm 3.7 ^{NS} a	14.7 \pm 10.4* a	17.3 \pm 9.1** a
LH/FSH	1.2 \pm 1.64	0.83 \pm 0.45 ^{NS} a	1.3 \pm 1 ^{NS} a	1.2 \pm 0.85 ^{NS} a

Values are expressed as mean \pm 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 ($P < 0.05$).

Figure (1) shows the correlation between time of lead exposure and serum testosterone levels in female workers. 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 (3) Distribution of female workers with hirsutism and miscarriages

Variables	Group I No. (%)	Group II No. (%)	Group III No. (%)	Total	Control
Hirsutism	2(14)	2(15)	3(25)	7(17.9)	0(0)
Miscarriages*	1(33)	3(50)	4(57)	8(50)	1(11)

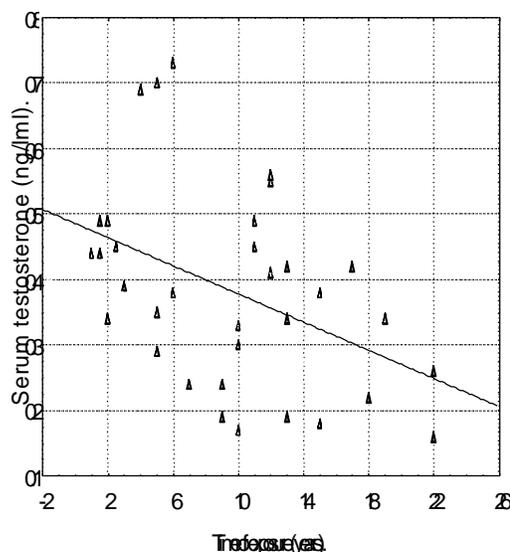


Figure (1) : Correlation between time of lead exposure and serum

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, clothes 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 $45 \mu\text{g}/\text{dl}$ 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 the raw materials.

The mean serum testosterone levels in all worker groups were significantly higher than that of control group ($P < 0.005$) (table 2). Figure (1) demonstrated a negative correlation between time of exposure to lead and serum testosterone levels in worker groups. The data showed an inverse relationship between time of lead exposure and serum testosterone levels, this may need further investigations to explain the correlation. The same results have been reported by Sokol-Rz⁽¹³⁾, where the rats treated with various doses of lead acetate for

more than 1 week exhibited a significant increase in Gonadotropine 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⁾.

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 serum 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 serum 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 $9 \mu\text{g}/\text{dl}$.

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 Rodamilans *et al.*⁽¹⁹⁾ who reported that in lead-smelter workers, serum LH levels are significantly raised, as compared with controls.

Furthermore Yen ⁽²⁰⁾ suggested that basal LH years 35 and continue to climb until several years after onset of menopause due to decrease negative feedback controls on production.

Ronis *et al.* ⁽²¹⁾ stated that, in female rats exposed to lead prepubertally, delay vaginal opening with more severe reproductive disruption, accompanied by suppression of circulating estradiol. Effects on circulating sex steroids were accompanied by variable effects on circulating LH levels, pituitary LH, and pituitary LH beta-mRNA. Increase in hypothalamic levels of Gn RHmRNA, and an increase in pituitary levels of LH mRNA and pituitary stores of LH in lead dosed animals. This increase due to lead disrupts the reproductive axis by interfering with feedback mechanisms at the hypothalamic and pituitary levels ⁽²²⁾.

In this study the results indicated that lead exposure has no effect on LH/FSH ratio in female workers. Elevated basal LH with an LH/FSH ratio >2 and some increase of ovarian androgen in an essentially non ovulatory adult women is presumptive evidence of polycystic ovary syndrome. A high serum FSH to LH ratio (1.9 to 3.8) has been observed in post menopausal women. Hypogonadism is usually associated with increased both FSH and LH levels; while decreased FSH and LH may occur in pituitary or hypothalamic failure ⁽²³⁾.

Table (3) showed high incidence of hirsutism (48%) in working women in batteries plant than in control group (0%). Also percentage of hirsutism in female worker groups increased with increasing exposure time to lead. Some of workers had hirsutism, their serum testosterone levels were high, and this type of hirsutism seems to be androgen induced hirsutism (hyperandrogenism). In this study in spite of decreased serum testosterone levels with prolonged exposure time (fig.1), percentage of hirsutism increased as time of exposure increased (table 3), so it can be concluded that hirsutism may depend on many factors other than androgen (testosterone) levels in female exposed to lead. When hirsutism is associated with obesity and menstrual abnormalities, the source of androgen excess is often ovarian, typically polycystic ovary syndrome. When it is associated with average weight and normal menses, the source is often adrenal and rarely (in <5% of cases) pituitary ⁽²⁴⁾. Table (3) showed increased incidence of miscarriages in female worker groups (50%) compared to control group (11%). Lead has toxic action on the trophoblastic epithelium and tonic contraction of the uterus. It therefore results either in abortion or a dead fetus ⁽²⁵⁾.

and FSH levels gradually rise after the age of

In this study when lead exposure time increased, percentage of miscarriages also increased (table 3). Much of the previous literatures focused on an increased incidence of spontaneous abortion and stillbirth associated with lead exposure in the workplace ^(25,26). Other studies have examined the issue of lead's involvement in spontaneous abortion, stillbirth, preterm delivery, and low birth weight. Women in the studies in Boston ⁽²⁷⁾, Cleveland ⁽²⁸⁾, Cincinnati ⁽²⁹⁾, and Port Pirie ⁽³⁰⁾ had average blood lead concentrations during pregnancy of 5-10 µg/dl; almost all had blood concentration less than 25 µg/dl. In the Cincinnati study, gestational age was reduced about 0.6 weeks for each natural log unit increase in blood lead concentrations. However, the Cincinnati and Port Pirie studies found a lead related decrease in duration of pregnancy, and Cincinnati and Boston studies reported a lead-related decrease in birth weight. In conclusion there are evident changes in sex hormones due to exposure of female workers to lead in Battery manufacturing plant.

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