

Impact of Mercury on Reproductive parameters in workers

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ABSTRACT

Mercury concentrations in blood and urine were estimated in workers exposed to chronic doses of elemental mercury, as well as plasma levels of LH, FSH, and testosterone. Comparisons of mean values of studied parameters were made between exposed workers and controls, and within exposed subjects of different categories. Mercury concentrations in both blood and urine were significantly higher in exposed workers than those of controls, and were even elevated in impotent individuals than in asymptomatic ones. However, there were no significant differences in plasma LH, FSH and testosterone levels in all groups. On the other hand, the correlation coefficient was positively significant between blood and urinary mercury concentrations, only in exposed and impotent individuals. More importantly, there was a negative correlation, between urinary mercury and testosterone concentrations in impotent subjects.

Key words: Mercury, Pollution, Hormones, Reproduction, Toxicity.

الملخص

لقد تمت معايرة تركيز الزئبق في كل من الدم و البول عند العمال المعرضين إلى جرعات مزمنة من الزئبق، بالإضافة إلى هرمونات (LH) ، (FSH) و تستوسترون في البلازما. أجريت مقارنة لمتوسطات المؤشرات المدروسة ما بين عمال معرضين و أشخاص استعملوا كشاهد، بالإضافة إلى المقارنة ما بين المعرضين المقسمين إلى أصناف مختلفة. سجل فرق معنوي في ارتفاع تركيز الزئبق في كل من الدم و البول

بين المعرضين و غير المعرضين، و كان اكثر ارتفاعا عند المصابين بالعقم عنه في المعرضين الذين لم تظهر عليهم أعراض التسمم. في حين لم يسجل أي فرق معنوي في تركيز (LH) ، (FSH) و تستوسترون عند كل الأفواج. من جهة أخرى فان معامل الارتباط ما بين تركيز الزئبق في الدم و البول كان معنويا فقط عند كل من المعرضين و عند المصابين بالعقم. الشيء المهم هو تسجيل ارتباط معنوي سالب ما بين الزئبق في البول و هرمون تستوسترون عند المصابين بالعقم.

مفتاح الكلمات. زئبق، تلوث، هرمون، تكاثر، تسمم

Introduction

Mercury is considered to have no biological roles in the organism. Thus, when found, mercury indicates a sign of pollution. Mining and smelting activities are the main sources of mercury intoxication. Depending on its levels, mercury affects cell metabolism at different degree, and that is due to its ability to distribute along all human tissues and, hence, accumulates in target organs, causing many physiological and biochemical disorders. Mercury vapor enters easily to the circulatory system through the lungs with inhaled air, in which 80 % is transported by the blood (Berlin, 1990). Because of its high affinity to proteins, mercury can be accumulated for a long time in brain, kidneys, testes, followed by the thyroid and the pituitary glands (Berlin, 1990; Magos, 1991).

Few reports concerning the effect of mercury vapor on male reproductive function have been published (Erfurth *et al.* 1990; McGregor & Masson; 1991; Barregard, *et al.*, 1994; Savitz *et al.*, 1994), and the physiological impairment of the gonado-pituitary axis are still not well understood.

The present study investigates the levels of mercury in blood and urine in male humans exposed to chronic mercury vapor in a mercury production plant. Luteinizing hormone (LH), follicle-stimulating hormone (FSH) and testosterone concentrations, have also been estimated, aiming to shed light on the possible effect, if any, of mercury intoxication on the gonado-pituitary axis.

Materials and Methods

Blood and urine samples were collected from 24 men of the Mercury Production Plant situated in Azzaba, Skikda. The individuals were subsequently divided into two sub-groups of twelve each. The first group includes men complaining from impotency, while those of the second group do not show any sign of clinical symptoms. However, for comparison, 21 other unemployed healthy men, living in the same region and from similar socio-economical class, have been used as controls and subjected to the same analytical procedure. Blood sampling was collected from brachial veins in heparinized glass syringes, in the morning, before being separated into polypropylene test tubes. One test tube was used for whole blood mercury analysis. The other was centrifuged at 3000 r.p.m. for 10 minutes, the plasma descanted, stored at -20°C till assayed for hormones. Plasma LH, FSH and testosterone levels were measured using a radio-immuno-assay (RIA) method, as previously described by Resenberg, 1979. On the other hand, about 10 ml of morning urine were collected from each worker and frozen till use, and that throughout the experimental period.

Inorganic mercury concentrations in both blood and urine were estimated using a Cold Vapor Atomic Absorption Spectrophotometer (Perkin Elmer 3030 B). Comparisons between mean values were made by student *t-test*. Correlation coefficients (*r*) were also calculated between some parameters.

Results

Table 1 represents all the studied parameters. However, a clear significant difference ($P < 0.001$) in mercury concentrations in both blood (B-Hg) and urine (U-Hg) has been recorded in exposed men compared to control individuals. However, no significant changes have been observed in plasma LH, FSH and Testosterone levels in either exposed or control subjects. Similarly, there was no significant difference in all parameters between impotent and asymptotic subjects. Moreover, there was a significant increase in B-Hg ($P < 0.01$) and U-Hg ($P < 0.05$) in impotent men compared to asymptotic individuals. The calculated correlation coefficient for the exposed workers was only positively significant for B-Hg against U-Hg ($r = 0.74$, $P < 0.001$). Meanwhile, the correlation was negative ($r = 0.63$, $P < 0.05$) between Hg-U and plasma testosterone in one side (figure 1), and was positive ($r = 0.76$, $P < 0.01$) between B-Hg and U-Hg in impotent individuals for the other side (figure 2). Finally, both FSH and age were negatively correlated ($r = 0.62$, $P < 0.05$) in asymptotic subjects.

Table 1. Plasma LH, FSH and testosterone concentrations (n mol/l), and mercury concentrations in blood ($\mu\text{g}/100\text{ ml}$) and in urine ($\mu\text{g} / \text{g.creatinine}$) in exposed (Impotents and asymptotics) and control subjects.

	Control ($\bar{X} \pm \text{SD}$, n = 21) (Range)	Exposed ($\bar{X} \pm \text{SD}$, n = 24) (Range)	Impotents ($\bar{X} \pm \text{SD}$, n = 12) (Range)	Asymptotics ($\bar{X} \pm \text{SD}$, n = 12) (Range)
Age (y)	39.62 $\pm$ 6.53 (32 – 53)	41.33 $\pm$ 6.43 (33 – 54)	42.25 $\pm$ 8.22 (33 – 54)	40.41 $\pm$ 4.12 (34 – 48)
Exposure (y)	-	14.79 $\pm$ 06.59 (6 – 27)	17.16 $\pm$ 7.82 (8 – 27)	12.42 $\pm$ 4.16 (6 – 21)
Hg-B	0.27 $\pm$ 0.17 (00 – 0.68)	5.96 $\pm$ 3.79 ^{a***} (2.2 – 11.8)	8.36 $\pm$ 4.06 ^{b**} (2.4 – 11.8)	3.58 $\pm$ 1.07 (2.2 – 4.8)
Hg-U	1.84 $\pm$ 1.39 (0 – 5)	178 $\pm$ 96.9 ^{a***} (56 – 420)	212.7 $\pm$ 121 ^{b*} (56 – 420)	143.4 $\pm$ 47.7 (60 – 200)
LH	4.54 $\pm$ 2.08 (1.34 – 8.64)	3.65 $\pm$ 1.51 (1.64 – 7.53)	3.88 $\pm$ 1.89 (1.64 – 7.53)	3.36 $\pm$ 0.78 (2.18 – 4.25)
FSH	4.65 $\pm$ 2.58 (1.15 – 9.64)	7.24 $\pm$ 4.78 (1.64 – 19.52)	7.90 $\pm$ 6.63 (1.64 – 19.52)	6.50 $\pm$ 1.72 (2.53 – 9)
Testosterone	18.14 $\pm$ 3.23 (13 – 24.2)	15.20 $\pm$ 4.68 (8.9 – 25.9)	14.77 $\pm$ 5.66 (8.9 – 25.9)	15.63 $\pm$ 3.65 (9.1 – 21.4)

a, control versus exposed; b, impotents versus asymptotics.

*, $P < 0.05$; **, $P < 0.01$, ***, $P < 0.001$

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*, P < 0.05; **, P < 0.01, ***, P < 0.001

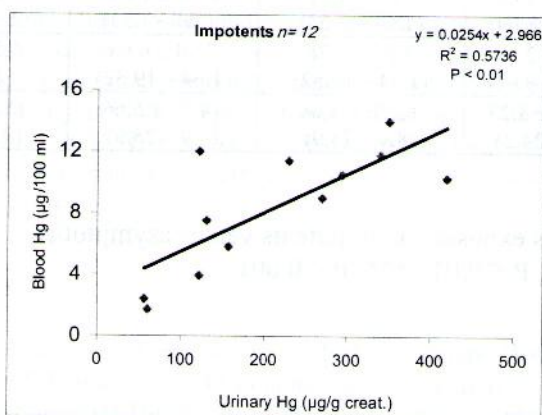
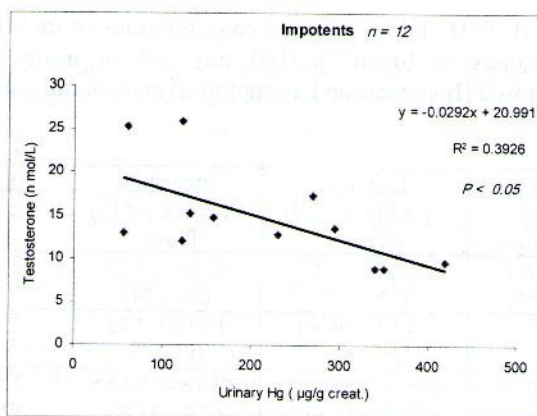


Figure legends.

Figure 1. The correlation coefficient (r) between plasma testosterone and concentrations (n mol / l) and urinary Hg ($\mu\text{g} / \text{g creatinine}$) in impotent workers ($n = 12$) exposed to mercury .

Figure 2. The correlation coefficient (r) between blood Hg ($\mu\text{g} / 100 \text{ ml}$) and urinary Hg ($\mu\text{g} / \text{g creatinine}$) concentrations in impotent workers ($n = 12$) exposed to mercury.

Discussion

According to the present results, it seems that the obtained mercury values in chronically exposed workers are in total agreement with those published by the World Health Organization, (W.H.O., 1980). Yet, although it is clear from the current investigations that there were remarkable variations in mercury concentrations in exposed men, no toxicological symptoms or clinical impairments were observed in some individuals.

It is of great interest, however, to note that mercury concentrations in both blood and urine are usually used as indicators for recent exposure, without refereeing to other organs (WHO, 1980). The anomaly in sexual function in this case is the most delicate side to assess, simply because it is a rather complex network in which endocrine system, nervous system and reproductive system are its main components. However, the observed impotency phenomenon in a great number of exposed workers is probably due to the accumulation of mercury in these organs. However, the brain is the main target organ for mercury toxicity, leading to the appearance of many symptoms, mainly the neuropsychological disorders, one of which is the decrease in libido. Consequently, it might directly affects organs producing hormones, since mercury has been found to accumulate in the pituitary gland (Magos, 1991). Additionally, mercury was reported to reduce testosterone biosynthesis in rat testes (Ng & Liu 1990). Paradoxically, no changes had been mentioned in testosterone levels in occupationally exposed workers (Barregard, *et al.*, 1994). On the other hand, this metal has been found in the seminal plasma of infertile men with a normal endocrine function (Chia, 1992). Moreover, the presence of mercury granules in testicular tissues of infertile men exposed to mercury vapor in working sites (Keck, 1993), might give the possibility of causing disturbances on cell metabolism, one of which is testosterone synthesis. The obtained negative correlation between urinary mercury and plasma testosterone concentrations in exposed impotent workers probably indicates that the flow of mercury into the kidney affect somehow the metabolism of this hormone. An increase in steroid excretion, the sex hormone precursors, was observed following an alteration in kidney function (Amdur 1991).

References

- AMDUR, M. O.; DOULL, J. & KLAASSEN, C. D. 1991.** Casarett and Doull's toxicology, the basic science of poisons. Third Edition, (Klaassen, C. D.; Amdur, M. O. and Doull, J.), p. 504-510, New York, Macmillan.
- BARREGARD, L.; LINDSTEDT, G. SCHULTZ, A. & SALLSTEN, G., 1994.** Endocrine function in mercury exposed chloralkali workers. *Occupational and Environmental Medicine*, **51**: 536-540.
- BERLIN, M., 1990.** Mercury. In "Handbook on the Toxicology of Metals" (L. Friberg; F. Norberg, and V. B. Vouk, Eds.) 2ed Ed., p 387-445, Elsevier, Amsterdam.
- CHIA, S. E.; ONG, C. N. LEE, S.T. & TSAKOK, F. H. M., 1992.** Blood concentrations of lead, cadmium, mercury, zinc and copper and human semen parameters. *Archives of Andrology*, **29**: 177-183.
- EIDE, R. & WESENBERG, G. R., 1993.** Mercury content of indicators and target organs in rats after long-term, low-level, mercury vapor exposure. *Environmental Research*, **61**: 212-222.
- ERFURTH, E. M.; SCHUTZ, A.; NILSSON, A.; BARREGARD, L. & SKERFVING, S., 1990.** Normal pituitary hormone response to thyrotrophin and gonadotrophin releasing hormones in subjects exposed to elemental mercury vapor. *British Journal Independent Medicine*, **47**: 639- 644.
- KECK, C.; BERGMANN, M.; ERNST, E.; MULLER, C, CLIESCH, S. & NIESCHLAG, E., 1993.** Autometallographic detection of mercury in testicular tissue of an infertile man exposed to mercury vapor. *Reproductive Toxicology*, **7**: 469-475.
- MAGOS, L., 1991.** Mercury metabolism and toxicology. In "Dental amalgam-a health hazard" (P. Horsted-Bindslev, L. Magos, P. Holmstrup, and D. Arenholt-Bindslev, Eds.), p 11-32. Munksgaard, Copenhagen.
- McGREGOR, A. J. & MASSON, H. J., 1991.** Occupational mercury vapour exposure and testicular, pituitary and thyroid endocrine function. *Human Experimental Toxicology*, **10**: 199-203.
- NG, T. B. & LIU, W. K., 1990.** Toxic effects of heavy metals on cells isolated from the rat adrenal and testis. *In Vitro Cell Devision Biology*, **26**: 24-28.
- RESEMBERG, E., 1979.** Immunoreactivity of standards and reference preparations used in the radioimmunoassay of follicle stimulating and luteinizing hormones in serum. *Journal Clinical Endocrinology*, **48**: 163-168.
- SAVITZ, D. A.; SONNENFELD, N. L. & OLSHAN, A. F., 1994.** Review of epidemiological studies of paternal occupational exposure and spontaneous abortion. *American Journal Industrial Medicine*, **25**: 361-383.

W.H.O., 1980. Recommended health-based limits in occupational exposure to heavy metals. Report of a WHO Study Group, *Technical Reproduction Series*, N° 647: WHO, Geneva.

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