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BRIEF REPORT

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Toxic effects of chronic occupational mercury vapor exposure on female workers of childbearing age

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Abstract

Background Few studies have been conducted on women of childbearing age with chronic mercury poisoning caused by mercury vapor exposure.

Methods Occupational exposure, clinical symptoms and signs, laboratory tests, auxiliary examinations, treatment, and follow-up of 31 female workers with chronic mercury poisoning from a mercury thermometer processing factory who received inpatient treatment at our hospital between September 2021 and August 2022 were analyzed.

Results In 31 female workers of childbearing age (23–43 years) who were chronically exposed to mercury vapor (3–31 months), urinary mercury levels exceeded the normal range. The clinical manifestations were primarily neurological (96.77%). Renal pathology of the two female workers suggested membranous nephropathy in the first stage. Some female workers experienced menstrual abnormalities, anxiety, depression, and sleep disorders. Treatment was mainly chelation therapy supplemented with antioxidants and other symptomatic supportive treatments. All patients achieved good results after discontinuing exposure to mercury vapor and receiving treatment. However, follow-up after discharge revealed that some female workers still had insomnia.

Conclusions Occupational mercury vapor exposure is hazardous to female workers of childbearing age and increases the risk of adverse effects on their reproductive health. Occupational protection and prevention of mercury exposure in female workers of reproductive age must be emphasized.

Keywords Mercury vapor, Occupational exposure, Women of childbearing age, Reproductive health

Introduction

Mercury is a metal, which can be toxic to humans, and is listed as one of the top ten chemicals of public health concern by the World Health Organization [1]. Mercury (Hg) exists in various forms: elemental (metallic), inorganic, and organic. At room temperature, elemental mercury can be volatilized into mercury vapor, which can then be inhaled [2]. Gold miners, dental personnel, and manufacturers of mercury-containing equipment are industries that pose the occupational risk of mercury exposure to workers [3]. As a large producer, emitter, and consumer of mercury, China is currently taking different measures to curb mercury pollution, according to the requirements of the Minamata Convention on Mercury [4]. Despite efforts to control mercury pollution, a few factories in the mercury-related industry continue to have indoor mercury air concentrations higher than the recommended levels owing to inadequate protection, resulting in occupational chronic mercury poisoning of workers. Accidental breakage

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of mercury-containing devices causes mercury vapor inhalation in daily life occasionally.

Mercury has toxic effects on several systems, including the neurological, renal, cardiovascular, immune, and endocrine [3, 5–7]. Various forms of mercury negatively affect the reproductive health of both sexes [8–10]. In women, elevated mercury levels are associated with an increased incidence of infertility, low fertility, menstrual and hormonal disturbances, and adverse pregnancy outcomes. Although some studies have examined the adverse effects of occupational exposure to mercury vapor on health, few have focused on the toxic effects in women of childbearing age.

To investigate the toxic effects of chronic mercury vapor exposure on women of childbearing age, we conducted a retrospective analysis of the clinical data of female workers of childbearing age with chronic mercury poisoning.

Methods

Study design and participants

We retrospectively collected and analyzed data from 31 female workers of childbearing age with chronic mercury poisoning at a mercury thermometer processing factory. The patients were hospitalized at our hospital between September 2021 and August 2022.

Data collection

Clinical information such as the patient's occupational history, clinical symptoms and signs, laboratory tests, auxiliary examinations, treatment, and follow-up was extracted from the electronic medical record system.

Clinical observation and treatment

Laboratory tests and auxiliary examinations

Blood and random urinary mercury levels were measured during the initial outpatient visit. Following the diagnosis of mercury poisoning, the patients were admitted to the hospital for treatment. On the first day of hospitalization, routine blood, routine urine, biochemical, and micro total protein (24-hour urine) tests were performed. During the chelation therapy, 24-hour urinary mercury levels were measured daily. Normal ranges for all laboratory test items in this article refer to our hospital's test reports, which may be slightly different for different laboratories. Additional tests were performed as needed based on the patient's condition, including chest radiography or computed tomography (CT) scans, head CT scans, electroencephalograms (EEG), and renal ultrasounds.

Psychological assessment

The psychiatrist used the Self-Rating Anxiety Scale and the Self-Rating Depression Scale to assess and provide treatment recommendations.

Treatment

The treatment of patients with mercury poisoning is based on chelation therapy (sodium dimercaptopropane sulfonate 0.25 g IM/QD). The dose was halved to drive mercury in patients with kidney damage. Each course of treatment was 3 days and discontinued 4 days before the next course of treatment. Each patient was hospitalized for two courses of treatment. During the treatment period, 24-hour urine samples were collected daily for mercury content measurement, and treatment was discontinued if the 24-hour urinary mercury concentration returned to normal. In addition, antioxidant therapy (glutathione 1.2 g Ivgtt/QD, silymarin capsules 0.14 g PO/BID) and other symptomatic treatments were supplemented.

Follow-up

Upon discharge, patients were informed that a follow-up visit to the outpatient was required in one month to assess their condition and mercury levels to determine whether to continue inpatient treatment.

Determination of mercury content

Blood mercury (normal < 0.015 mg/L), random urinary mercury (normal ≤ 2.25 μmol/mol Cr), and 24-hour urinary mercury (normal ≤ 45 μg/d) concentrations during chelation therapy were measured by hydride generation-atomic fluorescence spectrometry, and random urinary mercury was calibrated by measuring creatinine concentrations simultaneously.

Statistical analysis

The data obtained were statistically analyzed using SPSS 23.0, and categorical variables were expressed as the number of cases (percentage). Data that conformed to normal distribution were expressed as $\bar{x} \pm s$; data with skewed distribution were expressed as median (P_{25}, P_{75}).

Results

Baseline characteristics

All 31 female workers with chronic mercury poisoning were married and of childbearing age, with a mean age of

Table 1 Blood and random urinary mercury concentrations of 31 female workers on their first visit to our hospital

	Duration of stopping exposure			
	< 6 months		6–12 months	≥12 months
Received chelation treatment before n (n/31, %)	Yes 3 (9.68)	NO 10 (32.26)	NO 14 (45.16)	NO 4 (12.90)
Duration of exposure, months	20[a]	19.30 ± 5.96	8 (6.75,9.50)	6.25 ± 4.03
Duration of stopping exposure, months	2[a]	2.30 ± 2.11	7.43 ± 1.28	14.00 ± 2.83
Blood mercury concentration, mg/L, normal < 0.015	/	0.0028 ± 0.0015	0.0020 (0.0010,0.0025)	0.0015 (0.0010, 0.0020)
Urinary mercury concentration, μmol/molCr, normal ≤ 2.25	11.62 ± 4.05	40.95 ± 16.47	28.21 ± 10.34	29.11 ± 19.79

Data was presented as median (P_{25}, P_{75}), $\bar{x}\pm$ s, or n (%); /, not measured

[a] all three were exposed and stopped for the same duration

33.65 ± 4.99 years (range: 23–43 years), of whom 28 had given birth and three were not mentioned in the data.

History of occupational mercury exposure and body burden of mercury

All 31 female workers were employed by an individual enterprise and were engaged in work related to mercury thermometers. Their primary jobs included thermometer production, packaging, and quality control. Accidental breakage of mercury thermometers frequently occurred when workers carried out tasks such as marking, subdividing, and quality inspection. Broken mercury thermometers and scattered mercury beads were frequently observed near workbenches and floors. Some workers came into direct contact with mercury during cleaning work. They all worked indoors, with the larger workshops measuring 100 m^2 and the smaller workshops measuring 40–60 m^2. Larger workshops rely on natural ventilation through windows and ventilators, whereas smaller shops rely on natural ventilation through open windows with little effect. They worked 8–10 h a day, and only four of them wore masks for protection at work, with no other protective measures such as gloves or protective clothing. Their average work durations were 12.90 ± 7.22 months (range : 3–31 months).

When they approached our hospital, 27 workers were removed from the work environment and four were still working. Three workers had been treated with chelation therapy for a short period in another hospital, whereas the others had not received any treatment. The workers had normal blood mercury concentrations, but high urinary mercury concentrations (Table 1).

Clinical characteristics and auxiliary examinations

The clinical symptoms and abnormal signs that appeared after mercury exposure in the 31 female workers were dominated by the neurological system, with a high incidence of dizziness, headache, insomnia, and asthenia (Table 2). In addition to the common abnormalities in the digestive, respiratory, and renal systems caused by mercury poisoning, fewer common symptoms of hair loss were observed.

Menstruation was affected in seven of 31 patients (23%; random urinary mercury: 35.55 ± 13.25 μmol/molCr), with menstrual abnormalities manifesting as disturbed menstrual cycles ($n=4$), decreased menstrual flow ($n=4$), and dysmenorrhea ($n=1$). In addition, 10 of these 31 patients (32%; random urinary mercury: 22.78 ± 13.31 μmol/molCr) were evaluated by the Clinical Psychology Unit during hospitalization, which revealed anxiety ($n=5$), anxiety-depression ($n=3$), and sleep disorders ($n=2$).

Eight of 31 patients (26%) had decreased albumin (ALB; 37.8–39.9 g/L, normal values: 40–55 g/L), one (3%) had increased cholesterol (CHOL; 5.35 mmol/L, normal values < 5.18 mmol/L), two (6%) had increased low-density lipoprotein cholesterol (LDL; 3.40–3.66 mmol/L, normal values < 3.30 mmol/L), and four (13%) had decreased high-density lipoprotein cholesterol (HDL; 0.76–0.98 mmol/L, normal values > 1 mmol/L). Triglyceride (TG) and creatinine (Cr) levels were not elevated, and the liver function indices (glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase) were normal. Two patients were diagnosed with mercury-induced nephropathy, and renal biopsies from other hospitals revealed stage I membranous nephropathy in both cases. Laboratory results at our hospital were not consistent with nephrotic syndrome (Table 3). Renal ultrasound findings were normal in both patients.

Nineteen of the 28 patients (68%; random urinary mercury concentration: 30.58 ± 15.13 μmol/molCr) had abnormal chest radiographic findings, with the main abnormalities being slightly increased bilateral lung texture ($n=5$), increased bilateral lung texture ($n=13$), and

Table 2 Clinical manifestations and their corresponding mercury levels of 31 female workers

Symptoms and signs	n (n/31, %)	Random urinary mercury ($\bar{x}$± s,μmol/molCr)
Neurological	**30 (96.77)**	**(31.48 ± 15.41)**
Dizziness	15 (48.39)	
Headache	15 (48.39)	
Asthenia	13 (41.94)	
Insomnia	13 (41.94)	Easily agitated, irritable 11(35.48)
Memory loss	10 (32.26)	
Tremor		
Hand tremor	6 (19.35)	
Tongue tremor	2 (6.45)	
Palpebral tremor	1 (3.23)	
Blurred vision	3 (9.68)	
Dreaminess	2 (6.45)	
Joint pain	2 (6.45)	
Numbness of limbs	2 (6.45)	
Gastrointestinal	**18 (58.06)**	**(29.97 ± 18.31)**
Bleeding gums	8 (25.81)	
Nausea	5 (16.13)	
Dental ulcer	4 (12.90)	
Gum swelling	4 (12.90)	
Loss of appetite	3 (9.68)	
Vomiting	2 (6.45)	
Diarrhea	1 (3.23)	
Respiratory	**8 (25.81)**	**(32.49 ± 18.52)**
Cough	6 (19.35)	
Shortness of breath	4 (12.90)	
Chest tightness	4 (12.90)	
Expectoration	2 (6.45)	
Chest pain	1 (3.23)	
Nephrology	**6 (19.35)**	**(22.51 ± 14.08)**
Lumbago	4 (12.90)	
Lower limb edema	3 (9.68)	
Palpebral edema	2 (6.45)	
Foamed urine	2 (6.45)	
Others		
Alopecia	**3 (9.68)**	**(47.96 ± 11.84)**

pulmonary nodules ($n=2$). Eight patients who underwent thoracic CT showed abnormal findings; the main abnormalities were pulmonary nodules ($n=8$), inflammatory exudative changes ($n=1$), and pulmonary emphysema ($n=1$). Two patients with headaches had perfected head CT, and one had further perfected EEG, both of which had no abnormal findings.

Treatment outcome

Chelation therapy promoted urinary mercury excretion, and the maximum 24-hour urinary mercury concentration was 2066.4 μg/d in 31 female workers during treatment. Their 24-hour urinary mercury concentration gradually returned to normal levels. Nine patients developed allergic dermatitis during treatment with sodium dimercaptopropane sulfonate, which improved after anti-allergic treatment. After the patient developed allergic dermatitis, we immediately administered the diphenhydramine hydrochloride injection (20 mg IM). For mild cases, we continued chelation therapy and used antihistamines (loratadine 10 mg PO/QD or cetirizine dihydrochloride 10 mg PO/QN). For severe cases, all possible allergenic medications were discontinued, and glucocorticoids were added if necessary. Only one patient required glucocorticoid treatment (mometasone furoate cream Use. ext/BID; methylprednisolone sodium succinate for injection 40 mg + 0.9% sodium chloride injection 100 ml, Ivgtt/QD). After three days, the rash improved significantly. At the next hospitalization of the severe patient, we injected diphenhydramine hydrochloride injection (20 mg IM) before each chelating agent and also administered cetirizine dihydrochloride (10 mg PO/QN) during the chelation period. Two patients with membranous nephropathy were treated with chelation therapy without glucocorticoids and immunosuppressants and had a good therapeutic effect (Table 3). After treatment, the symptoms and signs of all the patients improved. Of the patients followed up in the outpatient, three still had insomnia 1 month after discharge and one 3 months after discharge. These four patients had normal urinary mercury concentrations during the retest.

Discussion

Here, we report the occupational exposure history, clinical symptoms and signs, laboratory tests, auxiliary examinations, treatment, and follow-up of 31 women of childbearing age who suffered from mercury poisoning due to chronic exposure to mercury vapor in a factory. We found that, more than a year after stopping mercury exposure, female workers who had been exposed to mercury vapor for a long time had high levels of mercury in their urine. The clinical manifestations were primarily neurological (96.77%). Renal pathology of the two female workers suggested membranous nephropathy in the first stage. Additionally, some female workers experienced menstrual abnormalities, anxiety, depression, and sleep disorders. All patients achieved good results after discontinuing exposure to mercury vapor and receiving treatment. However, post-discharge follow-ups revealed that some workers continued to experience insomnia after their urinary mercury levels returned to normal.

Table 3 Information of two female patients with mercury-induced nephropathy

	Case 1	Case 2
Age	37	32
Work on mercury thermometers	Production	Production
Personal protective equipment	No	No
Work duration (months)	20	11
Duration of stopping working (months)	2	7
Mercury treatment before our outpatient	Yes	No
Pathological stage of membranous nephropathy	Stage I	Stage I
Measurement of mercury content in our outpatient		
Blood mercury concentration (mg/L, normal < 0.015)	/	0.001
Random urinary mercury concentration (μmol/molCr, normal ≤ 2.25)	16.2	21.1
Renal clinical manifestations	Lumbago	Lumbago
	Palpebral edema	Lower Limb Edema
	Foamed urine	Foamed urine
Laboratory indicators before mercury treatment in our hospital		
ALB(g/L, normal: 40–55)	38.0	38.8
Blood lipid (CHOL, HDL, LDL, TG)	Normal	Normal
Cr (μmol/L, normal: 41–73)	44.6	41.4
M-TP24H (mg/24h urine, normal: 50–150)	12	395
Urine protein (normal: –)	(–)	(+)
Treatment outcome		
Renal clinical manifestations	No	No
24-hour urinary mercury level	Normal	Normal
M-TP24H (mg/24h urine, normal: 50–150)	/	175
Urine protein	/	(–)

Annotation: /, not tested; M-TP24H, micro total protein (24-hour urine)

Different forms of mercury determine the pathways of exposure, absorption, distribution, and target organ toxicity [2]. Elemental mercury is a liquid at room temperature but is highly volatile to mercury vapor, with occupational groups being the primary exposed groups. Elemental mercury has a low gastrointestinal absorption rate and limited dermal absorption, with inhalation of mercury vapor being the predominant route of exposure. Thirty-one female workers were chronically exposed to elemental mercury vapor because of a lack of protective equipment and spilled mercury beads in the work environment. Inhaled mercury vapor is rapidly absorbed and subsequently distributed to all tissues [2]. Mercury vapor can cross the blood-brain barrier. The main target organs are the brain and kidneys. Once mercury vapor enters the cell, it can be oxidized to form mercuric mercury. Urine is a useful indicator medium for renal mercury loading; however, no satisfactory indicator medium is available for the brain. Urinary mercury concentrations may also be an approximate indicator of systemic mercury loading because the kidneys tend to be a major site of mercury deposition. The patients in this study had normal blood mercury concentrations, but high urinary mercury concentrations. Untreated patients who had been out of the work environment for less than six months had higher blood and random urinary mercury concentrations than the other two groups due to the long duration of mercury exposure and short duration of separation. For organic mercury, whole blood is the preferred specimen because it is mainly concentrated in red blood cells [11]. In contrast, blood is useful for detecting inorganic mercury only when samples are collected shortly after exposure, due to its relatively short half-life of 2–4 days. Consequently, urine is a more reliable biomarker for longer-term exposure to elemental mercury vapor or inorganic mercury.

The central nervous system and kidneys are the main target organs of the toxic effects of long-term exposure to elemental mercury vapor [12]. The clinical presentation of female workers in our study was dominated by the neuropsychiatric system, followed by the digestive system, with a small proportion of the respiratory and renal systems. The primary clinical manifestations of

chronic mercury poisoning resulting from the inhalation of mercury vapor have been delineated in occupational histories as a triad of tremors, psychological disturbances (erethism), and gingivitis [2]. The neurological manifestations of the patients in this study were mainly dizziness, headache, insomnia, asthenia, easily agitated, irritability, memory loss, and tremors. A few patients presented with blurred vision, dreaminess, joint pain, and numbness of the limbs. Renal damage from mercury poisoning is often reported and may lead to nephrotic syndrome in severe cases; membranous nephropathy is a common pathology in patients with nephrotic syndrome [13, 14]. In our study, few patients had renal system symptoms; all patients did not have elevated creatinine. The two patients diagnosed with mercury-induced nephropathy showed the pathological pattern of membranous nephropathy but did not have nephrotic syndrome. These two patients did not have the highest random urinary mercury concentration among the 31 patients, which could be explained by the fact that mercury-induced nephropathy may result from a combination of direct injury and immune mechanisms [14]. Mercury poisoning leading to liver failure has been reported [15]. In this study, the gastrointestinal system manifestations in patients with mercury poisoning patients were mainly related to the gums, and liver function tests revealed normal results. Furthermore, if patients are acutely exposed to mercury vapor, they are likely to develop severe respiratory symptoms and alterations in lung imaging [16]. Nevertheless, in the present study, all patients were chronically exposed to low-dose mercury vapor; consequently, alterations in the chest imaging findings were not conspicuous.

In our study, some patients had menstrual abnormalities including irregular menstrual cycles, light periods, and painful menstruation. A substantial body of evidence suggests that inhalation of mercury vapor is associated with irregularities in the menstrual cycle [17]. The study on female workers exposed to mercury vapor has pointed out that mercury exposure is associated with perimenstrual symptoms and menstrual outcomes, and that dysmenorrhea may be a helpful biomarker for estimating female occupational mercury exposure [18]. A meta-analysis showed that occupational mercury exposure could lead to changes in a woman's menstrual period, cycle, and amount of menstruation; increase the incidence of painful menstruation; and affect pregnancy and the development of the fetus [19]. Regularity of the menstrual cycle is a crucial reproductive factor that indicates the overall health status of the population. Menstrual health has a mind-body connection because the menstrual cycle is regulated by the hypothalamic-pituitary-gonadal axis, which intersects the hypothalamic-pituitary-adrenal axis [20]. Mercury is an endocrine disruptor that can affect the hypothalamus, pituitary gland, ovary, adrenal gland, thyroid gland, etc [5, 21]. Elevated mercury levels have been linked to infertility and low fertility [10]. Because mercury vapor can pass through the placental barrier, pregnant women exposed to mercury vapor are at an increased risk of adverse reproductive outcomes [2, 22, 23]. Neurasthenic symptoms and mood changes were also observed in an analysis of the neurotoxic effects of mercury exposure on workers manufacturing thermometers [24]. In the present study, some patients experienced anxiety, depression, and sleep disorders. Notably, anxiety, depression, and sleep disorders may be detrimental to reproductive health [25–28]. Hair loss was also observed in a few patients in our study, which may have been related to the effects of mercury [29, 30].

Mercury poisoning treatment is dominated by chelating agents, such as the water-soluble sodium salt of 2,3-dimercapto-1-propane sulfonic acid (DMPS), which is the first-line treatment for acute and chronic conditions of inorganic mercury [31]. All patients in this study showed a significant trend of decreased urinary mercury concentrations and symptomatic relief after treatment. The two patients with mercury-induced nephropathy improved after chelation therapy alone, without the use of glucocorticoids or immunosuppressants. For patients with kidney disease secondary to mercury poisoning, discontinuation of mercury exposure and chelation therapy alone can achieve good results [13, 14]. During the outpatient follow-up after discharge, we found that insomnia persisted in some patients. Mercury vapor penetrates the blood-brain barrier and persists in the brain tissue for years [12]. Current chelating agents do not reduce mercury in the brain; therefore, they play a limited role in the neurological manifestations resulting from mercury vapor exposure [32].

Limitations

This study has a few limitations. First, it relied on workers' self-reported symptoms, which could be inaccurate due to recall bias. Workers might remember or report symptoms incorrectly, affecting the results. Second, there may be worried-well bias, where workers, knowing they were exposed to mercury, may report more symptoms because they are overly concerned about their health. The study also had a small sample size, which made it hard to apply the findings to a larger group. Finally, the study didn't include reproductive health-related laboratory and imaging tests, so it's hard to fully assess how mercury exposure might affect reproductive health.

Conclusions

Occupational mercury vapor exposure poses a health hazard to female workers of childbearing age and increases the risk of adverse reproductive health. Occupational protection and the prevention of occupational mercury exposure in female workers of childbearing age must be emphasized.

Abbreviations

CT	Computed tomography
EEG	Electroencephalograms
IM	Intramuscular injection
Ivgtt	Intravenous drip
BID	Twice a day
PO	Take orally
QD	Once a day
ALB	Albumin
CHOL	Cholesterol
LDL	Low-density lipoprotein cholesterol
HDL	High-density lipoprotein cholesterol
TG	Triglyceride
Cr	Creatinine
M-TP24H	Micro total protein (24-hour urine)
QN	Once a night
Us. ext	Use external

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Not applicable.

Authors' contributions

YP was involved in the study design, data collection and analysis, manuscript draft, and revisions. KQ was involved in data collection and analysis. HL and YS were involved in the study design and manuscript revisions. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Beijing Chao-Yang Hospital affiliated with Capital Medical University. Informed consent was not required because the study was retrospective with no harm to patients, and all case data were anonymized.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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