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ScienceDirect
Journal of the Chinese Medical Association xx (2017) 1−6
www.jcma-online.com

Original Article

Influence of seafood and vitamin supplementation on maternal and umbilical cord blood mercury concentration

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Received July 17, 2016; accepted November 3, 2016

Abstract

Background: The purpose of this study was to examine the influence of maternal seafood consumption and vitamin supplementation during pregnancy on maternal and umbilical cord blood mercury (Hg) concentration.
Methods: In this study of 145 healthy pregnant women (mean age 28.1 ± 5.2 years), we administered questionnaires, collected paired maternal/umbilical cord blood samples, and measured the anthropometrics of newborns. Blood Hg concentration was assayed by inductively coupled plasma-mass spectrometry.
Results: Sixty-one of these women (42.1%) used vitamins >3 times/wk prenatally. Seventy-eight of our study participants (61.9%) reported eating higher amounts of seafood during pregnancy. We found a strong correlation ($r = 0.76$, $p < 0.001$) between Hg levels in the paired maternal/umbilical cord blood samples. Mothers with high seafood consumption had a 2.91-fold greater risk (adjusted odds ratio 2.91, 95% confidence interval: 1.04−8.15, $p = 0.042$) of high Hg levels (>5.8 μg/L). However, mothers whose prenatal vitamin intake was >3 times/wk were found to have low Hg levels (≤5.8 μg/L) (adjusted odds ratio 0.06, 95% confidence interval: 0.01−049, $p = 0.008$).
Conclusion: High seafood consumption was an independent risk factor for high maternal Hg level, while vitamin supplementation was a protective factor. Further study is needed to investigate the specific effect of vitamins on Hg level.
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Keywords: mercury; pregnancy; seafood; vitamin

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.
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http://dx.doi.org/10.1016/j.jcma.2016.11.005
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Please cite this article in press as: Huang S-H, et al., Influence of seafood and vitamin supplementation on maternal and umbilical cord blood mercury concentration, Journal of the Chinese Medical Association (2017), http://dx.doi.org/10.1016/j.jcma.2016.11.005

1. Introduction

Mercury (Hg) is a toxic contaminant that can cross the placenta, and affect fetal growth and neurodevelopment.[1−3] Hg toxicity to the fetus became well known after high maternal exposure incidents occurred in Japan and Iraq.[2,3] Seafood consumption is the major source of Hg exposure for most people.[4] However, Hg exposure associated with seafood consumption may negatively affect neurodevelopment, although seafood rich in omega-3 fatty acids is associated with enhanced neurodevelopment.[5,6] This makes the potential harm of Hg exposure and the benefit of seafood consumption on health become important issues.

According to the cord blood levels reported in Budtz-Jorgensen et al's study,[7] the Environmental Protection Agency (EPA; USA) established a reference dose of 5.8 μg/L methyl Hg (MeHg) in blood for limiting exposure to MeHg in young children and women who are pregnant, are breast-feeding, or might be pregnant.[8] American pregnant women are advised to avoid fish with high Hg levels, but to eat 227−340 g/wk of a variety of fish low in Hg to support fetal growth and development.[9] This advice is complicated by the benefit of seafood rich in omega-3 fatty acids,[5,6] and Soon et al[10] reported that a significant portion of pregnant women in Hawaii consumed more than the recommended amount of seafood. Seafood is an important part of the Taiwanese diet and therefore a concern; however, seafood is only one part of the larger Taiwanese diet and should be evaluated with other nutrients in terms of mercuric intoxication. The protective effects of selenium, zinc, vitamin E, and vitamin B complex have been implicated in the alteration of Hg metabolism.[10,11] Most data about the protective effects of these nutrients are derived from animal research,[11] and therefore, implications of these data for human populations require further study.

Asian-American people and women of child-bearing age, who consume seafood more frequently than other race/ethic groups, have higher mean MeHg levels.[12,13] Taiwan is a large Asian island where people frequently consume seafood. Hsu et al's[14] study showed that 89% of pregnant women contain blood Hg exceeding the recommended value of 5.8 μg/L. Chien et al[15] demonstrated that the mean Hg concentration in hair was 1.73 ± 2.12 μg/g in Taiwanese women of child-bearing age, exceeding the EPA reference dose of 1 μg/g. These two studies[14,15] are consistent with previous studies reporting the risk of elevated Hg in Asians.[12,13] However, the data on the accumulation of Hg in pregnant women in Taiwan remain limited.[14,15] Therefore, in this study, we measured total Hg in paired maternal/neonatal blood samples, and further investigated the relationship between Hg levels and seafood as well as vitamin intake during pregnancy in Taiwan.

2. Methods

2.1. Participants and questionnaires

For this cross-sectional study, 145 healthy pregnant women with a mean age of 28.1 years were recruited from September 30, 2010 to May 25, 2011 in the Department of Obstetrics and Gynecology of Fooyin University Hospital in Dong Gang, Taiwan. The city of Dong Gang is a major seaside fishing area in southern Taiwan. The participants received a detailed explanation of the study procedures before consenting to participate. The research protocol was approved by the Institutional Review Board of Fooyin University (FYH-IRB-099-04-02-A). Written informed consent was obtained from all participants. Data on gestational age, prenatal examination results, and characteristics of the newborn were obtained from medical records. We used interviewer-administered questionnaires to collect information on demographic characteristics, smoking habit, alcohol drinking habit, betel-nut-chewing habit, use of Chinese medicine, seafood consumption, vitamin supplement, degree of education, etc. The semi-quantitative food frequency questionnaire was derived and modified from previously validated studies.[16,17] Content validity of the food frequency questionnaire was assessed by an expert panel consisting of six nutrition experts. After gathering opinions from the experts, questions without a precise content were excluded. The degree of seafood consumption was defined as the sum scores of seafood consumption items queried in the questionnaire. The score of seafood consumption was based on the answers to the following three questions. The first question was the following: "Approximately how many grams of fresh fish do you eat per day on average?" The following were the different response options to that question: (1) small amount, 0−30 g/d (1 point); (2) moderate amount, 31−60 g/d (2 points); (3) large amount, 61−90 g/d (3 points); and (4) large amount exceeding more than 90 g/d (4 points). The second question was as follows: "Approximately how many grams of shellfish do you eat per day on average?" The different response options to that question were the following: (1) small amount, 0−10 g/d (1 point); (2) moderate amount, 11−14 g/d (2 points); and (3) large amount, ≥15 g/d (3 points). The third question was as follows: "Approximately how many grams of canned seafood (fish or shellfish) do you eat per day?" The different response options to that question were the following: (1) small amount, 0−10 g/d (1 point); (2) moderate amount, 11−14 g/d (2 points); and (3) large amount, ≥15 g/d (3 points). The higher the sum sores, the greater the consumption of seafood. In our analysis, participants with 3 points were categorized into those people whose consumption approximated the EPA recommended ranges (227−340 g/wk). Those with scores over 3 were categorized into the high-seafood-consumption group whose consumption exceeded those recommendations. Those with ≤3 points were categorized into the less-seafood-consumption group. Anthropometric measurements of newborns were made by delivery room staff following standard procedures.

2.2. Blood sampling and sample analysis

Umbilical cord and maternal venous whole blood samples were separately collected into 9 mL standard laboratory-issued EDTA tubes. All samples were processed within 2 hours of delivery and stored at −80°C. Samples were sent to the

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Department of Biomedical Engineering and Environmental Sciences, Ultra Trace Micro-Analysis Laboratory at National Tsing Hua University, and were analyzed by inductively coupled plasma-mass spectrometry (7500ce; Agilent, Tokyo, Japan). The limit of detection for Hg was 0.353 μg/L (ppb). The intraday precision was tested with seven repeats of three samples of different concentrations. The average relative standard deviations were 0.49−0.71%. The interday precision was determined by analyzing the three samples three times every day, for 5 consecutive days. The average relative standard deviations were 1.01−2.76%, and the recovery was 98−102% of certified values.

2.3. Statistical analysis

Sociodemographic characteristics were analyzed descriptively. Hg concentrations in maternal blood (mHg) and that in umbilical cord blood (fHg) were described as mean ± standard deviation and categorized into 5%, 25%, 50%, 75%, and 95% percentiles. Pearson's correlation was used to analyze the association between Hg concentration in maternal and fetal blood. Receiver operating characteristic curve analysis was used for dichotomization of the frequencies of vitamin supplements. Multivariate logistic regression was performed to further analyze the association after controlling for race/ethnicity, education, cigarette smoking, alcohol drinking, betel quid chewing, Chinese medicine use, vitamin supplementation, and seafood consumption. Unadjusted odds ratios and fully adjusted odds ratios were reported. A p value of 0.05 was considered significant. All statistical analyses were performed using SAS (version 9.3; SAS Institute Inc., Cary, NC, USA).

3. Results

Between September 2010 and May 2011, 345 women visited the Department of Obstetrics and Gynecology of Fooyin University Hospital to receive third-trimester prenatal checkups (after 24 weeks). A total of 150 women were excluded because of chronic diseases (diabetes mellitus and hypertension), infectious diseases, twins, and stillbirth, leaving 195 eligible candidates. Fifty of these women did not want to participate in the study, leaving us with 145 participants, all of whom signed written consent forms. None of the mothers had complications during the study period, and only singleton infants were recruited into our study. These participants agreed to provide both samples of their own blood before delivery and cord blood samples at delivery, gave complete postpartum interviews, and allowed access to medical record data.

3.1. Characteristics of the study population

As seen in Table 1, the participants had a mean age of 28.1 ± 5.2 years, and prepregnancy and perinatal body mass indexes of 22.0 ± 3.3 kg/m^2 and 27.8 ± 3.9 kg/m^2, respectively. Almost 90% of the participants (84.8%) were of Han Chinese origin, with the remaining participants from various Southeast Asian countries. Almost half of the participants (49.0%) had graduated from high school. Of the participants, 9.0%, 7.6%, and 10.0% smoked cigarettes, consumed alcohol, and chewed betel quid during pregnancy, respectively. A minority (10.0%) of the participants said that they used Chinese herbal medicine within a month before birth. For logistic regression analysis of fHg, frequencies of vitamin supplements were dichotomized as low and high levels with the cutoff value (>2.5 times per week) based on the receiver operating characteristic curve analysis. Therefore, participants with vitamin supplements were categorized into two groups: those with vitamin intake >3 times/wk and those with vitamin intake ≤3 times/wk. Of all the women taking vitamins, 42.1% reported taking vitamin supplements >3 times/wk. A total of 126 women reported consuming seafood, with 61.9% being categorized into the high-seafood-consumption group. In total, these women gave birth to 71 female and 74 male neonates. Mean birth weight, birth length, head circumference, and chest circumference were 3081.6 ± 387.3 g, 49.6 ± 2.5 cm, 34.3 ± 1.4 cm, and 32.6 ± 1.6 cm, respectively. Most of the

Table 1
Maternal and neonatal characteristics (N = 145).

Characteristics	Mean ± SD or N (%)
Maternal characteristics	
Mean age (y)	28.1 ± 5.2
Race/ethnicity	
Taiwanese/Mainlander	123 (84.8)
Southeast Asians	22 (15.2)
Education	
Less than junior high school	32 (22.1)
High school	71 (49.0)
College degree	42 (29.0)
Prepregnant BMI (kg/m^2)	22.0 ± 3.3
Perinatal BMI (kg/m^2)	27.8 ± 3.9
Cigarette smoking	13 (9.0)
Alcohol drinking	11 (7.6)
Betel quid chewing	13 (9.0)
Chinese medicine	20(13.8)
Vitamin supplement	
>3 times/wk	61 (42.1)
≤3 times/wk	84 (57.9)
Seafood consumption (N = 126)	
High seafood	78 (61.9)
Less seafood	48 (38.1)
Neonatal characteristics	
Male sex	74 (51.0)
Birth weight	3081.6 ± 387.3 (1700.0−4040.0)
Birth length	49.6 ± 2.5 (41.5−55.0)
Birth head circumference	34.3 ± 1.4 (30.5−37.0)
Chest circumference	32.6 ± 1.6 (27.0−36.5)
Gestational age at birth	
Term (37−40 wk)	108 (74.5)
Post-term (>40 wk)	29 (20.0)
Preterm (< 37 wk)	8 (5.5)
Low birth weight (<2500 g)	
Yes	10 (6.9)
No	135 (93.1)

A total of 126 women answered how much seafood they consumed.
Taiwanese/Mainlander: Han Chinese; High seafood: intake score >3 points; Less seafood: intake score ≤3 points.
BMI = body mass index; N = number; SD = standard deviation.

neonates (74.5%) were full term, and only 10 (6.9%) had low birth weight (<2500 g).

3.2. Relationship between maternal and cord blood Hg concentration

Table 2 presents the distribution of Hg concentrations in maternal and umbilical cord blood samples. Mean mHg concentrations and fHg were 3.6 ± 3.9 μg/L and 5.0 ± 7.3 μg/L, respectively. Geometric mean mHg and fHg were 2.1 μg/L and 2.5 μg/L, respectively. Hg concentrations were about 1.4 times higher in umbilical cord blood than in maternal blood; mHg were strongly correlated with fHg ($r = 0.76$, $p < 0.0001$). The linear regression equation for the relationship between mHg and fHg was as follows: fHg = 1.405 × mHg − 0.068 (Fig. 1).

3.3. Effect of seafood and vitamin use on Hg level

As can be seen in Table 3, 29 mothers (20%) exceeded the US EPA reference dose (maximum acceptable dose of a toxic substance) of Hg in pregnancy (Hg > 5.8 μg/L). Han Chinese women did not have a significantly higher incidence of Hg > 5.8 μg/L than southeast Asian women [adjusted odds ratio (AOR) 1.48, 95% confidence interval (CI): 0.42–5.16, $p = 0.541$]. There was also no significant difference between subgroups with Hg > 5.8 μg/L or Hg ≤ 5.8 μg/L in terms of education level, cigarette smoking, alcohol drinking, betel quid chewing, and use of Chinese herbal medicine. Altogether, 97.5% of women taking vitamins >3 times/wk had Hg concentrations ≤5.8 μg/L, while 25.6% of those with high seafood consumption had maternal Hg levels of >5.8 μg/L. Women with vitamin intake >3 times/wk had a significantly lower incidence of Hg > 5.8 μg/L than those with vitamin intake ≤3 times/wk (AOR 0.06, 95% CI: 0.01–0.49, $p = 0.008$). On the contrary, women with high seafood consumption had a significantly higher incidence of Hg > 5.8 μg/L than those with low seafood consumption (AOR 2.91, 95% CI: 1.04–8.15, $p = 0.042$).

4. Discussion

In this study, we attempted to determine the effect of dietary sources on Hg levels in pregnant women. Our results showed that there was a strong correlation between mHg and fHg, and that prenatal vitamin use decreased the mHg. The effect of prenatal vitamin use on Hg levels in women during pregnancy is a very important finding.

Table 2
Data on Hg levels in maternal blood and umbilical cord blood ($n = 145$).

Parameter	Mean ± SD, GM	Percentiles				
		5%	25%	50%	75%	95%
Mercury (μg/L)						
Maternal Hg (mHg)	3.6 ± 3.9, 2.1	0.4	1.0	2.2	5.0	12.7
Fetal Hg (fHg)	5.0 ± 7.3, 2.5	0.5	1.1	2.3	5.4	17.3

fHg = mercury concentration in umbilical cord blood; GM = geometric mean; mHg = maternal mercury concentration; SD = standard deviation.

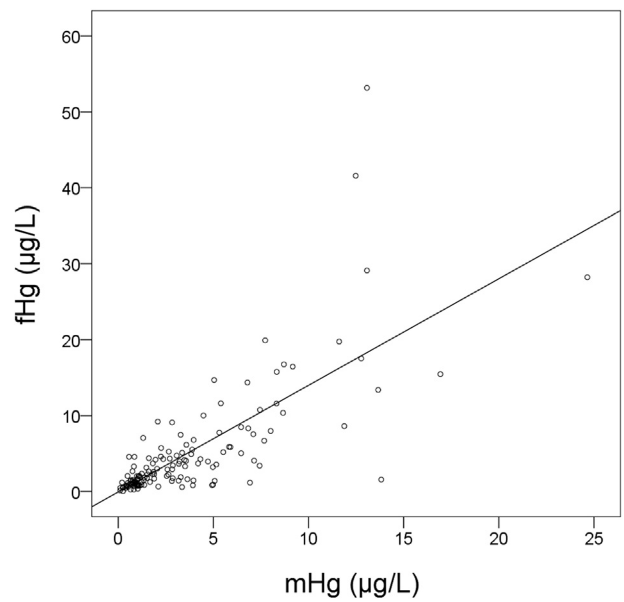

Fig. 1. Association between mercury levels in maternal blood and cord blood; $r = 0.76$, $n = 145$, $p < 0.0001$.

The geometric mean of the mHg in this series was 2.1 mg/L, a value much lower than that reported in 2007 in a study of pregnant Taiwanese woman (8.6 mg/L).[14] Hsu et al[14] reported 89% of the mHg exceeded 5.8 μg/L. However, in the current study, 20% of mother's blood samples exceeded 5.8 μg/L. Two reasons may explain the discrepancy of Hg levels between Hsu et al's[14] and our studies. First, the study period used in two investigations was quite different. Additionally, their study[14] was performed 7 years prior to ours. In recent years, pregnant women in Taiwan have been educated about the potential risk of Hg toxicity associated with seafood consumption. Second, our sample size ($n = 145$) was larger than that in Hsu et al's[14] study ($n = 65$). Small sample size might be associated with an underpowered analysis.

Compared with the geometric means reported for other countries, our participants had higher blood concentrations of Hg at the time of delivery than pregnant women in Canada (0.48 mg/L),[18] Poland (0.83 mg/L),[19] and the USA (1.6 mg/L).[20] By analyzing data from the 2011–2012 US National Health and Nutrition Examination Survey, Mortensen et al's[12] study showed that Asians had higher MeHg concentrations. Buchanan et al[13] further reported that Asian women of childbearing age, who consumed seafood more frequently than other race/ethic groups, had higher mean MeHg levels. In Taiwan, fish consumption during pregnancy is generally higher than that found in other countries because traditionally it is thought that eating fish during pregnancy makes for better nutrition for the neonate.[14] Taiwanese studies,[14,15] including our investigation, are in agreement with the previous studies reporting the risk of elevated Hg in Asians.[12,13]

Our result showed a strong correlation of Hg in maternal and umbilical cord blood of paired maternal/neonatal samples. The component transport between umbilical cord and maternal serum is very complex.[21] Usually, fHg is higher than mHg due to its high affinity for fetal hemoglobin.[22] Previous studies,[3,14]

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Table 3
Logistic regression analysis of Hg levels in maternal blood ($N = 145$).

Variables of mother	Hg ≤ 5.8 μg/L ($n = 116$)	Hg > 5.8 μg/L ($n = 29$)	COR[a] (95% CI)	p	AOR[b] (95% CI)	p
Race/ethnicity						
Southeast Asians	17 (77.3)	5 (22.7)	1.00		1.00	
Taiwanese/Mainlander	99 (80.5)	24 (19.5)	0.82 (0.28−2.46)	0.729	1.48 (0.42−5.16)	0.541[c]
Education						
Less than junior high school	26 (81.3)	6 (18.8)	1.00		1.00	
High school	57 (80.3)	14 (19.7)	1.06 (0.37−3.08)	0.908	1.32 (0.39−4.41)	0.658[c]
College degree	33 (78.6)	9 (21.4)	1.18 (0.37−3.75)	0.777	1.73 (0.45−6.60)	0.425[c]
Cigarette smoking						
No	107 (81.1)	25 (18.9)	1.00		1.00	
Yes	9 (69.2)	4 (30.8)	1.90 (0.54−6.68)	0.316	3.01 (0.58−15.77)	0.191[c]
Alcohol drinking						
No	106 (79.1)	28 (20.9)	1.00		1.00	
Yes	10 (90.9)	1 (9.1)	0.38 (0.05−3.08)	0.364	0.37 (0.04−3.22)	0.367[c]
Betel quid chewing						
No	104 (78.8)	28 (21.2)	1.00		1.00	
Yes	12 (92.3)	1 (7.7)	0.31 (0.04−2.48)	0.270	0.51 (0.06−4.65)	0.546[c]
Chinese medicine use						
No	99 (79.2)	26 (20.8)	1.00		1.00	
Yes	17 (85.0)	3 (15.0)	0.67 (0.18−2.47)	0.549	0.87 (0.16−4.68)	0.867[c]
Vitamin supplement						
≤3 times/wk	77 (73.3)	28 (26.7)	1.00		1.00	
>3 times/wk	39 (97.5)	1 (2.5)	**0.07 (0.01−0.54)**	**0.011**	**0.06 (0.01−0.49)**	**0.008**[d]
Seafood consumption						
Less seafood	42 (87.5)	6 (12.5)	1.00		1.00	
High seafood	58 (74.4)	20 (25.6)	2.41 (0.89−6.53)	0.083	**2.91 (1.04−8.15)**	**0.042**[e]

Taiwanese/Mainlander: Han Chinese; high seafood: intake score >3 points; less seafood: intake score ≤3 points. Values in bold font were statistically significant. AOR = adjusted odds ratio; CI = confidence interval; COR = crude odds ratio; SD = standard deviation.
[a] The p value is estimated by logistic regression.
[b] The p value is estimated by multivariate logistic regression.
[c] AOR is adjusted for vitamin supplement and seafood consumption in 126 pairs of infants and mothers.
[d] AOR is adjusted for seafood consumption in 126 pairs of infants and mothers.
[e] AOR is adjusted for vitamin supplement in 126 pairs of infants and mothers.

including our investigation, have also documented higher Hg levels in cord blood than in maternal blood. Although there was no significant association of Hg level and birth outcome in this study, Hg has been reported to be associated with developmental delay in children whose mothers were exposed to it during pregnancy.[23,24] This raises the question as to how much seafood a pregnant woman can eat without the risk of Hg toxicity. A Taiwanese study by Chien et al[25] showed that 21.6−24.3% and 45.6−57.4% of the daily Hg dose estimates exceeded the reference dose for typical and high seafood consumers, respectively.[25] Their analysis suggested that the acceptable ingestion rate of fish for women during childbearing is 90.8 ± 15.7 g/d.[25] As advised by the Food and Drug Administration and EPA in 2014, pregnant woman should eat 227−340 g of a variety of fish each week from choices that are lower in Hg content.[9] Further studies are required to elucidate the optimal dose of fish during pregnancy in the Asian race.

According to our multiple logistic regression analysis, the status of prenatal vitamin use significantly decreased the mHg. It is an interesting issue about whether vitamins or dietary modifications may be used to modify Hg intoxication. Metabolized MeHg produces active oxygen species (superoxide radicals, hydroxyl radicals, singlet oxygen, and peroxides), so vitamins E and C, which have antioxidant properties, may modify MeHg toxicity.[11] In a study by Al-Attar,[26] administration of vitamin E was found to protect against heavy metal-induced renal and testicular oxidative stress and injuries in male mice. Another different study by Al-Attar[27] reported that vitamin E protected against the heavy metal-induced liver injury in albino mice, suggesting that the attenuating effect of vitamin E might be due to its antioxidant activity. Abd El-Aziz et al[28] reported that vitamin E might ameliorate some aspects of MeHg developmental toxicity in rat fetuses. Kim et al[29] also found a negative association between serum folate and blood Hg concentrations in pregnant Korean women. Their findings suggest that folate is associated with the blood Hg level through its participation in the Hg detoxification process.[29] These previous findings[26−29] may partially explain the effect of prenatal vitamin use on decreasing maternal levels of Hg. The effect of vitamin use on heavy metals in pregnant woman still requires further investigation.

This study had several limitations. One is that it was a single-center investigation of pregnant woman utilizing a modest sample size. Another limitation is that the contents of vitamins used by the participants in this study were not studied in detail.

In conclusion, our results showed a positive correlation between mHg and fHg, and that high seafood consumption was an independent risk factor for a high maternal Hg level.

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Although an association between prenatal vitamin supplementation and reduced maternal Hg level was found, the protective effect of vitamin supplementation to modify Hg toxicity requires further detailed study.

Acknowledgments

Part of this work was supported by grants from Kaohsiung Veterans General Hospital (VGHKS104-83, VGHUST104-G7-7-3, VGHKS105-106, and VGHUST105-G3-1-3) and Kaohsiung Medical University (MOST104-2314-B-037-012-MY2 and MOST105-2632-B-037-002).

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