การรับสัมผัสสารปรอทจากสิ่งแวดล้อมกับการเปลี่ยนแปลงของพุทธิปัญญา

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บทคัดย่อ

หนึ่งในสารที่ทราบกันดีว่ามีความเป็นพิษต่อระบบประสาท คือสารปรอท ซึ่งเป็นโลหะหนักที่มีความเป็นพิษและพบได้ในสิ่งแวดล้อม โดยเฉพาะในรูปของ methylmercury โดยอาหารทะเลเป็นแหล่งหลักของการรับสัมผัสของ methylmercury งานวิจัยทางด้านผลกระทบของปรอทกับความผิดปกติของความสามารถของสมอง (Cognitive impairment) มีจำกัดในคนไทย ดังนั้นวัตถุประสงค์ของงานวิจัยนี้ เพื่อหาความสัมพันธ์ระหว่างระดับปรอท กับการเปลี่ยนแปลงของระดับพุทธิปัญญา (Cognitive function) โดยผู้เข้าวิจัย จำนวน 436 คน อายุระหว่าง 45-65 ปี การวิเคราะห์ระดับปรอทในเลือดใช้ inductively coupled plasma mass spectrometry (ICP-MS) และประเมิน cognitive function ด้วยแบบประเมิน Montreal Cognitive Assessment (MoCA) ค่าเฉลี่ยของระดับปรอทของกลุ่มการศึกษาเท่ากับ 5.12 ไมโครกรัมต่อลิตร ระดับปรอทในเลือดเพิ่มขึ้นตามความถี่ของการบริโภคปลาที่มีไขมันปานกลาง นอกจากนี้ระดับปรอทในเลือดมีความสัมพันธ์กับการลดลงของระดับพุทธิปัญญาโดยเฉพาะในส่วนของความจำ โดยสรุปการศึกครั้งนี้พบแนวโน้มความสัมพันธ์ ที่สามารถอธิบายการรับสัมผัสปรอทกับการเกิดความผิดปกติทางด้านความสามารถของสมอง นอกจากนี้งานวิจัยในส่วนกลไกระดับเซลล์ที่เกี่ยวข้องกับความเป็นพิษต่อระบบประสาทจากปรอท การประเมินการรับสัมผัสที่เหมาะสม และการศึกษาบทบาทของสารอาหารจากธรรมชาติหรือการเสริมสารอาหาร เพื่อลดความเสี่ยงหรือผลกระทบต่อสุขภาพ เป็นเรื่องสำคัญที่ควรดำเนินการต่อไป

คำสำคัญ: ปรอท การรับสัมผัสจากสิ่งแวดล้อม พุทธิปัญญา

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Environmental Mercury Exposure and The Alteration in Cognitive Function

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Abstract

One of the best known neurotoxins is mercury (Hg). It is a ubiquitous environmental toxicant that cause long-lasting neurological and developmental deficits in animals and humans, especially in the form of methylmercury (MeHg). MeHg is accumulated in fish, which represent a major source of human exposure. The researches related to effects of Hg exposure on cognitive dysfunction in Thai people are limited. Therefore, the purpose of this study was to investigate the associations between blood mercury, influencing factors, and cognitive function. The study population included 436 individuals, aged between 45-65 years old. Their blood mercury levels were measured by inductively coupled plasma mass spectrometry (ICP-MS). Cognitive impairment was evaluated by Montreal Cognitive Assessment (MoCA). The geometric means of blood mercury were 5.12 μg/L. Blood mercury was higher in subjects who more frequently ate fish with medium amounts of fat. Decline in cognitive function, especially in the memory domain, was observed in individuals with the third tertile of blood mercury level. In conclusion, the potential relationship between mercury exposure and cognitive impairment was partly indicated in this findings. Further studies with particular emphasis on molecular mechanisms of Hg-induced neurotoxicity, appropriate exposure assessment tools together with the potential protective role of natural or dietary supplement should be emphasized.

Keywords: Mercury, Environmental exposure, Cognitive function

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Introduction

Mercury (Hg) is a ubiquitous toxic heavy metal in environments. The toxicities of Hg are different, depending on their forms including elemental, inorganic and organic Hg. Generally, some Hg forms are emitted into the environment from anthropogenic and natural sources. They can be converted to methylmercury (MeHg) by microorganisms, which will enter the food chains and bioaccumulate in long-lived predatory marine fishes. Non-occupational population are mainly exposed to Hg through seafood consumption (in the form of MeHg). Previous studies reported that consumption of fishes and seafood was positively associated with the blood and brain Hg levels[1,2]. Ninety-five percent of MeHg in food has been easily absorbed and distributed throughout the body. It can also transport across the blood brain barrier which result in induction of neurotoxicity[3]. Previous study in low level of MeHg exposure through fish consumption were associated with increasing in hair Hg concentration and neuropsychological dysfunction [4]. Another common form of Hg which possibly be exposed is an elemental mercury released from a dental amalgam. It is a mixture of metals which is consisted of liquid (elemental) mercury, silver, tin, and copper. There are several forms of Hg that released from amalgam fillings: elemental mercury vapor, metallic ions, and/or fine particles. Low levels of mercury, in the form of a vapor, can be inhaled and absorbed into the lungs[3]. It has been reported that high levels of mercury vapor exposure were associated with adverse effects in the brain and the kidneys. A longitudinal study showed the association between removal of dental amalgam and urine mercury. The mean urine mercury level of participants with one or more amalgam surfaces was higher than those with no dental amalgam (1.61 μg/g-creatinine and 0.78 μg/g-creatinine, respectively)[5].

Neurotoxicity is the hallmark of MeHg exposure. Understanding of Hg metabolisms, such as absorption, distribution, storage, biotransformation and elimination is crucial for better understanding of molecular mechanisms related to Hg-induced neurotoxicity. Various mechanisms have been purposed previously including disruption of the antioxidant system of glutathione (GSH), dyshomeostasis of glutamate and calcium ion at the synapse of neuron, and binding to thiol groups or sulfhydryl (i.e. glutathione peroxidase, thioredoxin reductase and selenoprotein). Consequently, these cellular disturbances can lead to excessive generation of reactive oxygen species and neurodegenerative diseases [6,7].

These toxicities of Hg may be silent for a latency period or can develop cognitive impairment as well as neurodegenerative disease [8,9]. Furthermore, the nervous system of elderly people is more vulnerable to neurotoxic agents. Neurocognitive domain include language, learning and memory, social cognition, complex attention, executive function and perceptual-motor function. Cognitive impairments are problems of memory loss and impaired cognitive ability. Basically, cognitive impairment, includes mild cognitive impairment (MCI) and dementia, are age related disorders. MCI is an intermediate clinical state between normal cognitive aging and dementia, characterized by objective and subjective memory loss. The Montreal Cognitive Assessment (MoCA) is a well-established cognitive screening, highly sensitive at differentiating MCI from normal cognition and dementia and is widely validated against the most commonly used instrument, the Mini-Mental State Examination (MMSE)[10]. Thai version of MoCA has been already available[11]. Thailand is going to be the aging society with given the longer life expectancy, a dramatic increase in the prevalence of cognitive dysfunction is anticipated. For this reason, investigating on environmental mercury exposure in the older adults is considered as an important health concerned. Thus, the aims of this study were (1) to investigate the level of mercury in blood and various influencing factors on its level and (2) to examine the association between blood mercury and its effect on cognitive function.

Materials and Methods

Study subject

The 436 subjects (with aged 45-96 year old) were participated in the fourth survey of the Electric Generating Authority of Thailand (EGAT) which has been conducted in 2013. The EGAT study was one of the cohort studies of chronic disease that was focused on multidisciplinary researches related to risk factors of cardiovascular disease (CVD), including nutrition and toxicology. Data of self-administered questionnaire, physical examination and biochemical analysis were performed in this study. Information obtained from the questionnaires included personal characteristics (e.g., gender, age, height, weight, occupational history, and tooth-filling frequency), lifestyle (current alcohol intake and tobacco usage), medical history (including history of neurological diseases such as migraine, polyneuropathy, epilepsy, and Parkinson’s disease). Dietary assessment related to the frequency of seafood and fish consumption were evaluated. Exclusion criteria for this study were: (1) abnormal biochemical parameter, liver function, kidney function, (2) incomplete data for the MoCA, (3) history of cognitive impairment e.g. dementia, Parkinson disease and (4) incomplete data for the general characteristic and laboratory. Ethical document for this research was approved by the Committee on Human Rights Related to Researches Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital, in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All participants gave their informed consent before they were included in this study.

Blood mercury analysis

Blood mercury concentration were analyzed by using inductively coupled plasma mass spectrometry for total mercury (Agilent 7700x ICP-MS, Agilent technology). The method used for the determination of total mercury in blood samples was based on a previous publication described by Gajek et al.[12]

Biochemical measurement

Fasting glucose concentration, HbA1c, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, and homocysteine enzymatic assay were analyzed by an automated analyzer (COBAS ®C8000, Roche).

Cognitive assessment

Neuropsychological assessment was performed by the well-trained trained research staff by using the Thai version of Montreal Cognitive Assessment (MoCA).[11] This version is divided into 7 cognitive domains, including visuospatial/executive (5 points, 3 items: trails B test, cube copy and clock drawing), naming (3 points, 1 items: confrontation naming (lion, hippo, camel)), memory (5 points, 5-trial recall of 5 items with short-term delayed recall), attention (5 points, 3 items: digits forward and backward, tapping the letter 1 in letter list and serial subtraction), language (3 points, 2 items: sentence repetition and categorical verbal fluency), abstraction (2 points, 1 items: similarities), and orientation (6 points, assessment of orientation to time and place). Scores range from 0 to 30 points, with a lower score reflecting higher decline of cognitive impairment. The cut-off point is 26. Add one point for an individual who has 12 years or fewer of formal education.

Questionnaire of dietary pattern

Seafood consumption was categorized by type (fish or seafood) and by frequency of consumption (0-1 time/month, 1–2 day/week, more than 3 day/week). The seafood types were divided into 5 groups; for instance, 1) shell 2) shrimp and squid, 3) fish with low amount of fat (2-4g/100g fish), such as mackerel, king mackerels, black pomfret, snapper, 4) fish with medium amount of fat (4-8 g/100g fish), such as snakeskin gourami, silver barb, white pomfret, and 5) fish with high amount of fat (9-20g/100g fish), such as snakehead fish, striped catfish, catfish, black-banded kingfish.

Statistical analysis

The probability distributions of the continuous variables were analyzed by using the Kolmogorov-Smirnoff test. Continuous data were expressed as mean ± SD and statistical analyzed by parametric methods. Blood mercury was log-transformed and expressed as geometric mean and 95% confidence interval (CI). The independent t-test and ANOVA were used to evaluate the differences of means between two groups and among three groups, respectively. All tests were two-tailed, and statistical significance was considered by an alpha level of 0.05 or less. The statistical analysis was conducted by using SPSS statistic version 21.0 for windows (SPSS, Inc., Chicago, IL).

Result

The main characteristics of subjects and the biochemical parameters, classified by gender, are presented in Table 1. The participants consisted of 436 Thais. There were 284 males (65%) and 152 females (35%) with the average age of 57.6±4.2 and 58.0±4.4 years old, respectively. The means of BMI, systolic and diastolic blood pressures were 24.8±3.7 kg/m^2, 138.2 ±16.2 mmHg and 81.1 ± 9.8 mmHg, respectively. Most of these participants had educational level of more than12 years (75.7%). Alcohol consumption was 76.7% of drinkers and the most frequency (38.8%) was less than 1 time/month. A total of 13.5% of participants were current cigarette smokers with the most frequency (89.8%) smoked daily. Only 4 female subjects have been reported as smokers. Percentage of participants with amalgam filling were 68% of total population. Significant differences of the average of clinical biochemical variables, total cholesterol, HDL-cholesterol, triglyceride, homocysteine, and blood mercury level between gender have been observed. For biomarker of exposure, the geometric mean of blood Hg in all study participants was 5.12 µg/L (range from 0.83 to 43.65 µg/L). Blood Hg level in male was significantly higher than female (male=5.4 µg/L vs female=4.65 µg/L, *p*=0.032).

Table 1 General characteristics and biochemical variables of the study population

Characteristics	Total (N=436)	Males (N=284)	Females(N=152)
Age, years	57.7±4.3 (49-65)	57.6±4.2 (49-65)	58.0±4.4 (49-65)
Body Mass Index (BMI)(kg/m^2)	24.8±3.7	24.6±3.3	25.2±4.2
SBP, mmHg	138.2±16.2	138.9±16.4	136.9±15.9
DBP, mmHg	81.1± 9.8	82.3± 9.6	78.8± 9.9
Educational level (N)			
• <12 years	24.3% (106)	21.5% (60)	30.3% (46)
• ≥12 years	75.7% (330)	78.9% (224)	69.7% (106)
Alcohol consumption (N)	309	239	70
Nondrinkers, % (N)	23.3% (72)	21.3% (51)	30.0% (21)
Drinkers, % (N)	76.7% (237)	78.7% (188)	70% (49)
Frequency of alcohols consumption, % (N)			
• Everyday	9.3% (22)	11.2% (21)	2.0% (1)
• 5-6 days/week	8.9% (21)	10.6% (20)	2.0% (1)
• 1-4 days/week	17.3% (41)	20.7% (39)	4.1% (2)
• 1-3 days/month	25.7% (61)	27.1% (51)	20.4% (10)
• > 1 time/month	38.8% (92)	30.3% (57)	71.4% (35)
Amalgam filling, % (N)			
• Yes	68% (295)	64.7% (183)	74.2% (112)
• No	32% (139)	35.3% (100)	25.8% (39)
Smoking cigarette, % (N)			
• Nonsmokers	86.5% (377)	80.6% (229)	97.4% (148)
• Smoker	13.5% (59)	19.4% (55)	2.6% (4)
- <1 day/week	5.1% (3)	5.5% (3)	0% (0)
- 1-6 day/week	5.1% (3)	5.5% (3)	0% (0)
- Everyday	89.8% (53)	89.1% (49)	100.0% (4)
Glucose, mg/dL	102.5±27.6	104.3±29.3	99.3±24.1
HbA1C, %	5.91±1.09	5.93±1.19	5.86±0.89
Total cholesterol, mg/dL	218.8±44.7	213.8±44.6	228.2±43.6**
HDL cholesterol, mg/dL	56.8±15.6	53.7±14.9	62.6±15.2**
LDL cholesterol, mg/dL	144.8±39.9	142.4±40.1	149.5±39.1
Triglyceride, mg/dL	151.5±109.7	162.4±122.6	131.1±76.4**
Homocysteine, µmol/L	13.9±5.2	15.1±5.7	11.8±3.3**
Blood mercury (GM and 95%Cl), µg/L	5.12 (4.79-5.47)	5.4 (4.98-5.85)	4.65* (4.17-5.19)

*, ** Significant difference from male with $p<0.05$ and $p<0.001$, respectively.

Various influencing factors related to blood mercury level; cigarette smoking, alcohol consumption and amalgam filling, were also investigated, as demonstrated in Figure 1. Mean blood mercury level was significantly higher in the group of 45-55 years old than those with 56-65 years old (5.65 µg/L vs 4.88 µg/L, *p=0.038*). Although blood mercury level of individuals with amalgam filling was a slightly higher than those without amalgam filling. However, it did not reach statistical significance. Other possible contributing factors observed in this study such as BMI, cigarette smoking and alcohol consumption did not affect the blood mercury levels.

The association of dietary patterns related to mercury sources and blood mercury levels were depicted in Figure 2. The results showed that blood mercury levels tended to be associated with higher frequency of dietary pattern, such as shell, shrimp, squid, and fish with low and medium amounts of fat. Furthermore, blood mercury levels significantly increased in participants with consumption of fish with medium amount fat (frequency of 0-1 time/month, 1-2 day/wk, more than 3 day/wk, were 4.66, 5.55 and 6.1 µg/L, respectively $p<0.007$).

Prevalence of cognitive impairment in the study subjects (aged 45-65 year old) was 42% and mostly found in individuals with educational level of less than 12 years (55.7%). Total score and each domain of MoCA, classified by educational levels were investigated with tertiles of blood mercury levels (T1: GM=2.47 µg/L, range: 0.83-3.89; T2: GM=4.98 µg/L, range: 3.9-6.6; T3: GM=10.92 µg/L, range: 6.61-43.65), as presented in Table 2. The MoCA scores only in individuals with education of more than or equal to 12 years were significantly decreased in the 3rd tertile of blood mercury (25.5 ± 2.7 score) when compared with the 2nd tertile (26.7 ± 2.5 score, $p<0.05$). In addition, mean score of memory domain among subjects with the 3rd tertile blood mercury was statistically lower than those in the 2nd tertile of blood mercury (3.05±1.66 vs 3.58 ±1.62, $p<0.05$).

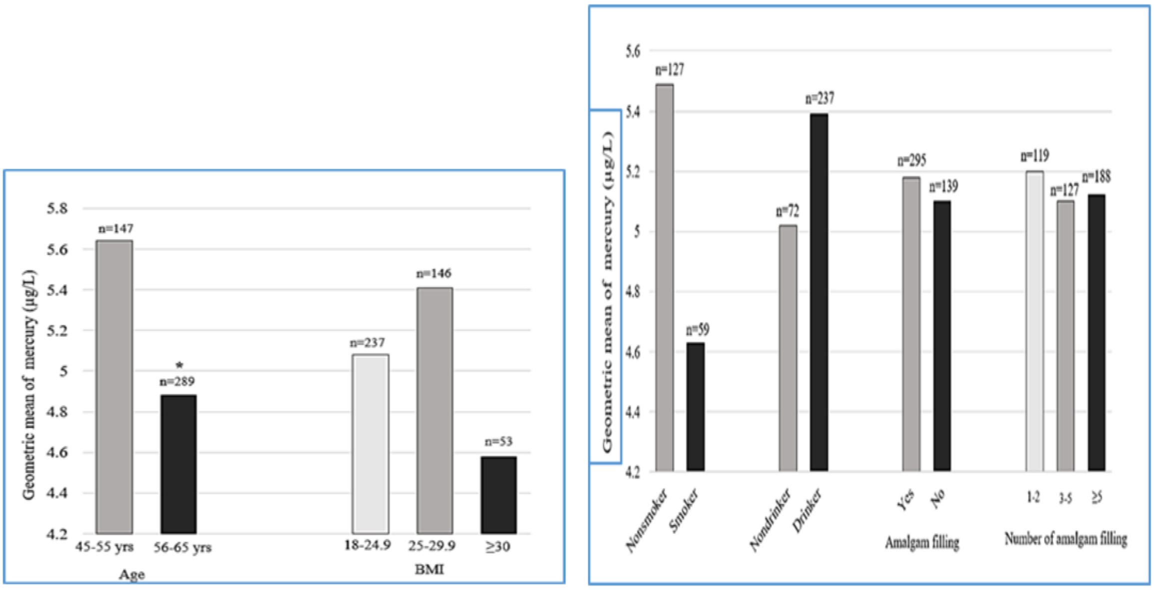

Figure 1 Blood mercury level classified by different factors

(*Significant difference from 45-55 years with p<0.001)

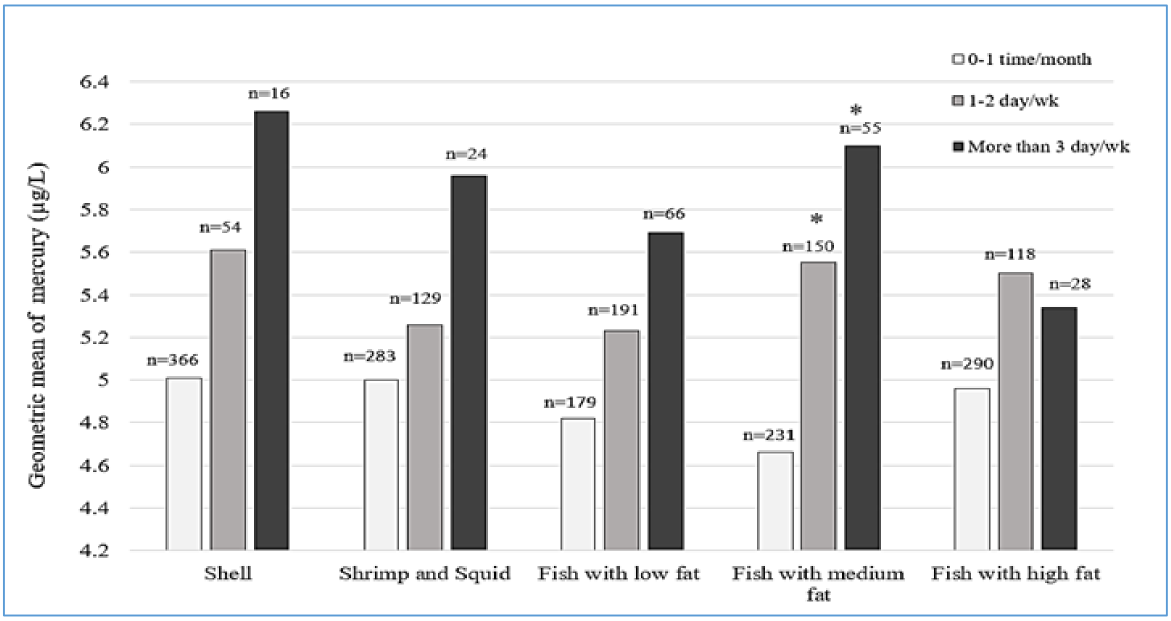

Figure 2. Blood mercury level classified by type and frequency of seafood and fish consumption

(* Significant difference from 0-1 time/month with p<0.05)

Table 2 Mean of MoCA scores in each tertiles of blood mercury classified by educational levels

Cognitive domain	Tertiles of Hg	MoCA score	
		Education, <12 years	Education, ≥12 years
Visuoexecutive/5	1	3.82±1.16	4.74±0.57
	2	4.14±0.88	4.72±0.57
	3	3.95±1.15	4.55±0.81
Naming/3	1	2.95±0.23	2.98±0.14
	2	2.93±0.26	2.98±0.13
	3	2.82±0.45	2.98±0.14
Attention/6	1	5.05±1.35	5.65±0.66
	2	5.14±0.99	5.72±0.60
	3	5.26±1.19	5.67±0.6
Language/3	1	1.08±0.94	1.81±1.03
	2	1.38±0.94	1.87±1.03
	3	1.31±0.95	1.66±0.96
Abstraction/2	1	1.26±0.86	1.67±0.61
	2	1.28±0.84	1.78±0.51
	3	1.38±0.78	1.62±0.7
Memory/5	1	3.21±1.65	3.23±1.63
	2	2.97±1.64	3.58±1.62
	3	2.93±2.06	3.05±1.66*
Orientation/6	1	5.89±0.39	5.93±0.59
	2	6.00±0.00	5.99±0.09
	3	6.00±0.00	6.00±0.00
Total	1	23.8±4.3	25.9±3.0
	2	24.4±2.9	26.7±2.5
	3	24.1±3.9	25.5±2.7*

* Significant difference from the 2nd tertile with p<0.05

(T1: GM=2.47 μg/L, range: 0.83-3.89; T2: GM=4.98 μg/L, range: 3.9-6.6; T3: GM=10.92 μg/L, range: 6.61-43.65)

Discussion

Mercury is one of the global health concerns since acute or chronic mercury exposure can cause adverse effects during any period of life. Basically, three forms of mercury: mercury vapor from amalgam tooth fillings, methylmercury in fish, and divalent mercuric salts, are the most widespread of this metal exposures. Mercury can enter the food chains and bioaccumulate in fish[14]. General population are commonly exposed to MeHg through seafood consumption and dental amalgam filling[(3)]. The geometric mean of blood mercury levels in this study population was 5.12 μg/L, which ranged from 0.83 to 43.65 μg/L. Forty-one percent of the participants had blood mercury levels above the U.S. EPA reference (5.8 μg/L)[14]. As reported by the previous studies, blood mercury levels investigated in this study was comparable with those observed in Korean general population (4.15 μg/L, 95% CI;3.93–4.38 μg/L), which were reported by the Third Korean National Health and Nutritional Examination Survey (KNHANES III) in 2005[15]. Moreover, our finding indicated the lower blood mercury levels than those observed in non-occupational Taiwanese (9.64 μg/L)[(16)]. However, blood mercury levels reported in this study is higher than those observed in the US population (0.99 ± 0.04 μg/L), which were reported by the National Health and Nutrition Examination Survey (NHANES) in 2007–2010[(17)].

Several demographic and lifestyle determinants of blood mercury were identified. Geometric means of blood mercury levels were significant different according to sex, age and fish and seafood consumption. The results of this study indicated that blood mercury level was higher in male (5.4 μg/L) than in female (4.65 μg/L), as depicted in Table 2. Similar finding was reported in general population of Korean study (male: 4.70 μg/L, female: 3.70 μg/L)[14]. In contrast to the results of the study in Czech Republic (male: 0.78 μg/L, female: 0.94 μg/L)[18] and in New York city, USA (male: 2.67 μg/L, female: 2.78 μg/L)[18], blood mercury level was higher in female than in male. Proposed explanations for this evidence might be related to demographic, lifestyle (i.e. alcohol consumption), geographic, and dietary factors.

Another factor that affected blood mercury level was age (Figure 1). Our result indicated that the blood mercury level was higher in the 45-55 years old subjects (5.64 μg/L) than the 56-65 years old subjects (4.88 μg/L). This might cause by physiological alteration in the elderly people. Hemoglobin level in the 56-65 years old subjects (Hb=13.9 g/dL) were lower than those observed in the 40-56 years old subjects (Hb=14.3 g/dL). Thus, binding of mercury with red blood cells in the elderly people may diminished[16]. McKelvey et al. (2007) also reported that blood mercury level was higher in 40-59 years (3.23 μg/L) than 60 years and over (2.71 μg/L)[19]. Similarly, KNHANES III showed that the blood mercury level decreased in Korean older people[15].

It is generally accepted that seafood represents one of the major sources of mercury in the human food chain. Marine organisms are able to accumulate this metal and its most toxic organic compounds by filtering their food from sea water. The US.FDA has investigated the level of mercury contamination in commercial fish and shellfish in 1990-2012[20]. In Thailand, mercury concentration in marine fish were also reported [21-23]. The total blood mercury level are usually used as a biomarker of exposure and generally represent the recent exposure of MeHg from dietary intake[24]. The NHANES study in 2007-2010 has reported the data from food frequency questionnaire and blood mercury level of 10,673 adults and their findings demonstrated that blood mercury levels increased with the frequency of seafood consumption[17]. Another published study also showed that blood mercury level were increased roughly 3.7 times in the individuals who consumed fish or shellfish more than 20 times per month when compared to the persons who did not consume those kinds of food[18]. Moreover, consumption of oily fish can cause increasing of blood mercury level higher than white fish consumption[25]. This study showed that the geometric means of blood mercury levels tended to be increased with the increasing of frequency of consumption of shell, shrimp, squid, fish with low (2-4 g/100g fish) and medium amount of fat (4-8 g/100g fish). In particular, blood mercury level was significant difference in group of high consumption of fish with medium amount of fat. The example of fish with medium amount of fat were bluefish, catfish, rainbow trout, and swordfish[26]. Swordfish was reported that had high mercury level and were limited to consume of pregnancy[27]. We had expected to underline the association between participants with higher intakes of seafood and levels of blood mercury in a dose–response manner. However, our results could partly indicate that MeHg concentration in seafood might be varied in the different areas due to the geographic variation such as temperature and pH of water and quantity of mercury in water. In addition, blood mercury level may vary due to pattern of fish consumption, fish species, geographic variation, region of residency, race and socioeconomic status[28].

Dental amalgam is mainly composed of elemental mercury and widely used as a tooth filling material. People may expose to small amount of mercury vapors during the placement and removal of amalgam. Inorganic mercury which can be converted from elemental mercury are also possible to release while drinking hot liquid and eating sour foods[3]. Its target organ are nervous system and kidney. Zwicker et al. (2014) reported that mercury level in urine was higher in individuals with dental amalgam filling than the person who have never filled with dental amalgam[5]. However, there was no correlation observed between the number of amalgam filling and blood mercury level in this study (Figure 2). Similar to another study, Eyeson et al. (2010) also demonstrated that the mercury level in blood and urine were not correlated with chronic toxicity of mercury from restoration of amalgam of patients[29].

The most well-known health hazard from mercury exposure is an adverse effect on neural tissue. The capability of mercury to readily cross the blood/brain barrier allows it access to the brain and central nervous system. Cognitive impairment include mild cognitive impairment (MCI) and dementia, that is an age related disorder. The present findings demonstrated that prevalence of MCI in Thai elderly people with aged 45-65 year old was 42% which was more than those observed in the study of Wangtongkum et al. (2008) with 5.63% in 1492 of Thai people (aged over 45 years) in Chiang Mai by using Thai Mini Mental State Examination (TMSE)[30]. In addition, the prevalence of MCI in menopausal women at HRH Princess Maha Chakri Sirindhorn Medical Center was 16.7 % by using Thai MoCA with 24 of cut point score[31]. The present study demonstrated that total score and most of domain in MoCA tests were significantly associated with education and age which were confirmed by several studies[10,32]. The educational level was related to socioeconomic status and health habits such as poor diet which can alter cognitive performance[33]. For age factor was similar to the study of Thanupat et al. (2013) which indicated that age of individual with MCI (65.9 years) were higher than individual without MCI (61.9 years) in in menopausal women[31].

Chronic mercury exposure can cause neurotoxicity that may be silent for a latency period and can develop the cognitive impairment as well as neurodegenerative disease that were confirmed by in vitro and in vivo studies[3,8,9]. Furthermore, the nervous system of elder people are more vulnerable to neurotoxic agents. Hock et al. reported that Alzheimer's patients had elevated levels of mercury in blood [34]. In present study, the result showed that the 3rd tertile of blood mercury level had lower total MoCA score than the 2nd tertile in ≥12 years of education levels. Moreover, the sub scores of cognitive domain, memory domain, were significantly decreased as the blood mercury level increased in ≥12 years of education in this study. The finding showed that the significant variables that have the effects on cognitive impairment were age, education and mercury level, respectively. According to Yokoo et al. (2003) study, low level exposure of MeHg from fish intake in adult can alter performance on neuropsychological test of verbal learning, memory, fine motor speed and dexterity and concentration[4]. In addition, Weil et al. suggested that elevated blood mercury concentrations from seafood consumption was associated with worse visual memory and better manual dexterity in Baltimore older[35]. However, highly intake of fish and seafood was associated with mercury levels in brain, the correlation between these levels and neuropathology were not observed [2]. Similarity, Johansson et al. demonstrated that no association between blood mercury level and cognitive function, assessed by MMSE, was found in Sweden population with mean age of 87 year old[36]. The mechanisms of mercury induced neurotoxicity might be induction of oxidative stress, disruption of glutathione antioxidant system, dyshomeostasis of glutamate and calcium at the synapse of neuron.

This is the first study that aimed to investigate the association between mercury and cognitive impairment in Thai population by using MoCA test, a good cognitive screening tests and widely used in epidemiological study. However, there were some limitations in the present study. A cross-sectional study conducted in this research might not represent the cause-effect of the association between mercury and cognitive impairment. In addition, fish and seafood intake levels were evaluated by using the non-quantitative FFQ questionnaire, there might be some possibility of misclassification. There are inadequate data of amalgam filling such as number and surface areas of amalgam fillings and how long of the period of filling with amalgam.

In conclusion, since the aging population may be particularly vulnerable to neurotoxicants, this study was an attempt to examine whether this rapidly growing group is sensitive to even lower levels of mercury exposure. Since the blood mercury levels in our study did not absolutely appear to be associated with adverse neurobehavioral effects. But the results suggest that these levels of mercury exposure may present a concern for older adults. Studies with more detailed dose assessment are necessary to confirm this conclusion since a single blood-mercury level may not be an optimal estimate of cumulative dose. A large-scale prospective studies with detailed dietary information, especially fish and seafood items, are warranted to make a definitive conclusion. Further study on genetic polymorphisms related to toxicodynamic and toxicokinetic influences of Hg on individual susceptibility to cognitive dysfunction should be investigated.

Conflict of Interests

The authors declare no conflict of interests.

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