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Methylmercury bioaccumulation in rice and health effects: A systematic review

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Abstract

Methylmercury (MeHg) is highly toxic. Rice can accumulate high levels of MeHg. Rice is the staple food of more than half of the world's population; therefore, MeHg exposure via rice consumption has become a global emerging issue. This article reviews the rice Hg concentration in the world, the bioaccumulation mechanism of MeHg in rice, the human Hg exposure from rice consumption, and health effects. It is found that rice Hg concentrations from non-contaminated areas around the world are generally within the safe intake range. Most MeHg in rice is found in edible white rice since MeHg in rice plants can form the MeHg–Cys complex (MeHg-cysteine), which can be transferred into rice grain during maturation of rice. Exposure to MeHg through rice consumption can reduce antioxidant activity and damage the nervous system in rats and may cause children's intelligence decline.

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Rice, Methylmercury, Bioaccumulation, Human exposure, Health effect.

Introduction

Methylmercury (MeHg) is a toxic compound, and the developing central nervous system is particularly vulnerable to MeHg [1]. The general population is mainly exposed to MeHg through fish consumption [2]. Meanwhile, rice can be another source of MeHg exposure [3–5]. Rice cultivated in the Wanshan Hg mining area can bioaccumulate MeHg, and the MeHg concentrations in rice grain were found to be as high as 174 ng/g [5,6]. Rice consumption can be the main pathway of MeHg exposure for local populations in the Guizhou mercury (Hg) mining area, which contributed >95% of total MeHg intake [5,7]. Rice grain as the staple food does not have the beneficial nutrients such as n-3 fatty acids found in fish tissues; therefore, the dose–response relationship of human MeHg exposure from rice consumption and health effect may be different from that observed in the fish-eating populations [8,9]. Rice is the staple food of more than half of the world's population [10], but the research on human MeHg exposure via rice consumption is relatively limited. Since the Minamata Convention on Hg entered into force in 2017, the evaluation of human Hg exposure via diet intake is crucial for risk control [11]. Due to the large population of potential exposure, the high frequency of daily intake, and the absence of beneficial ingredients, the rice Hg study is particularly important for understanding the current situation of global human Hg exposure. This article reviews the rice Hg concentration in the world, the bioaccumulation mechanism of MeHg in rice, the human Hg exposure from rice consumption, and health effects.

Rice Hg concentration in the world

Horvat et al. (2003) [12] found that MeHg concentration in rice grains can reach up to 145 ng/g in the Wanshan Hg mine in Guizhou province, China. Generally, Hg concentrations in rice grain in the nonpolluted area were less than 20 ng/g, and inorganic Hg is the main form of Hg in the rice (Table 1). By the national survey conducted in 15 provinces across China, rice total mercury (THg) and MeHg concentrations indicated relatively low levels, and overall means were 4.74 ng/g (1.06–22.7 ng/g, n = 560) and 0.682 ng/g (0.03–8.71 ng/g, n = 560) for THg and MeHg, respectively [3]. The means of rice THg concentration in Bangladesh and Europe were 2.48 ng/g (0.42–14.4 ng/g) and 3.04 ng/g (0.53–11.1 ng/g), respectively [13,14].

Notably, high THg levels of rice were observed in gold and Hg mines. The rice THg concentration in the Wanshan Hg mining area ranged from 1.3 to 166 ng/g with a mean of 14.0 ng/g, and 37% exceeded the national limit suggested by the Chinese National Standard Agency [19]. The averages of rice THg and MeHg concentrations in the Wuchuan Hg mining area were 26.8 ng/g (6.0–113 ng/g) and 7.8 ng/g (3.1–13.4 ng/g),

Table 1

Rice Hg concentrations in different study areas (ng/g).

Study area	THg	MeHg	Polluted area or not	Reference
Bangladesh	2.48 (0.42~14.4)	0.83 (0.026~7.47)	–	[13]
England, France, Swiss	3.04 (0.53~11.1)	1.91 (0.11~6.45)	–	[14]
Guiyang, China	3.70 (1.1~9.4)	2.0 (0.4~3.6)	No	[15]
Punjab and Sindh, Pakistan	4.51 (0.44~157)	3.71 (0.16~67.85)	–	[16]
China	4.74 (1.06~22.70)	0.682 (0.03~8.71)	–	[3]
Hunan, China	5.7 (2.0~22)	2.4 (1.7~3.8)	Coal-fired power plant	[17]
Gaohong, China	10.6 (1.3~41.2)	5.29 (0.09~21.5)	Fluorescent lamp manufacturing area	[18]
Wanshan, China	14.0 (1.3~166)	6.1 (0.29~65)	Hg mine	[19]
Mindanao, Philippines	20.0 (1.00~43.0)	–	Gold mine	[20]
Wuchuan, China	26.8 (6.0~113)	7.8 (3.1~13.4)	Hg mine	[21]
Karnataka, India	38.3 (26.0~58.0)	–	–	[22]
Xiushan, China	47.5 (12~384)	12.1 (9.2~64)	Hg mine	[23]
California, USA	50.4 (50.0~50.9)	4.6 (4.1~5.0)	Gold and Hg mines	[24]
Lombok Island, Indonesia	–	57.7 (10.6~115)	Gold mine	[25]

respectively. The MeHg constituted a large portion of Hg in rice, which was up to 40.2% on average [21]. Moreover, the average of the rice MeHg level was as high as 57.7 ng/g (10.6–115 ng/g) in gold mines in Lombok island [25]. Since gold extraction by the amalgamation method and Hg mining activities will cause serious environmental Hg pollution in these areas [24,25]. Rice samples showed Hg contamination around the coal-fired power plant (5.7 ng/g), fluorescent lamp plant (10.6 ng/g), and chemical plant (14.6 ng/g), but these concentrations were significantly lower in those in gold and Hg mines [12,17,18].

Bioaccumulation mechanism of MeHg in rice

Bioaccumulation factors for MeHg in rice were on average more than 800 times higher than those for IHg, which showed that rice grain is an intensive bioaccumulator of MeHg [26]. The moist environment of rice growth provides a favor living environment for anaerobic microorganisms. Soil IHg can be methylated by these bacteria (e.g. iron-reducing bacteria, sulfate-reducing bacteria, and methanogens), then MeHg can be absorbed and accumulated by the rice plant [27]. Most MeHg in the rice plant is distributed in rice grain, whose rice seeds contained more 77% of total MeHg in the rice plant [28]. Furthermore, most MeHg in rice grain is found in edible white rice [29]. Unlike rice IHg, which can come from the atmosphere, paddy water, and soil, the main source of MeHg in the rice plant is the soil [30,31]. The accumulation process of MeHg in the rice plant is different from IHg [32]. IHg can chelate with phytochelatins (PCs), an enzymatically synthesized cysteine-rich peptide, to form the Hg–phytochelatin complex during the accumulation of IHg in the rice plant, and then, most of IHg is retained in the root of rice [29,32,33]. This is also an important detoxification process of the IHg reaction in rice. Nevertheless, soil MeHg can be absorbed by the root to form the MeHg–Cys complex (MeHg–cysteine); the structure of the MeHg–Cys complex closely resembles that of methionine, a large neutral amino acid, which enables MeHg to enter the above-ground part of the rice plant [34]. During rice plant growth, soil MeHg can be transferred through roots to leaves and stalks, and most of the MeHg in leaves and stalks is enriched into rice grain during maturation of rice [29,35]. In addition, the bioaccumulation of MeHg in rice is the result of the combination of methylation and demethylation in rice [36]. The net methylation potential can partly impact the rice MeHg concentrations. A recent research found that the rice plant may have a self-defense process that demethylation of MeHg occurs in growing rice, but the process of methylation and demethylation in the rice plant is still not clear, and more researches are needed [37].

Human MeHg exposure from rice consumption

Rice consumption can be the main pathway of human MeHg exposure in the Wanshan mining area, Guizhou province, and even in southern inland China [5,38–40]. Using Hg stable isotope geochemistry, an effective tracer of human “fingerprint” exposure and metabolic processes, it was also found that MeHg exposure of Wanshan residents mainly originated from rice diet [40]. Rice consumption contributed >95% of MeHg intake for local residents in Guizhou province, China [38]. For inland areas or Hg-contaminated areas, the MeHg exposure via rice consumption has become a non-negligible pathway of human MeHg exposure. In addition, globalization has expanded the impact of human MeHg exposure via rice consumption through the international rice trade. In 2013, globalization caused 9.9% of human MeHg exposure via the international rice trade and significantly aggravated rice-derived exposure in Africa (62%), Central Asia (98%), and Europe (42%) [4].

Human MeHg exposure via rice consumption can be assessed by MeHg concentrations in different types of biological samples. Blood Hg and hair Hg are the most commonly used biomarkers of Hg exposure [41]. Blood reflects a recent exposure of 1−2 half-lives (50−70 days). Blood Hg concentrations will increase rapidly during or after brief exposures [34,41]. Blood Hg concentration in the general population is less than 5.8 μg/L. The hair sample can represent the average Hg exposure level throughout the growing period. Simultaneous hair Hg enables dynamic tracking of Hg exposure, as the hair growth rate is estimated to be 1 cm/month [41]. The hair sample is the more suitable biomarker for exposure assessment in large-scale epidemiological studies because sample collection and storage are simple and practical [41,42]. Hair Hg concentration in the general population is less than 1 μg/g [43].

Hair THg concentrations among different populations are summarized in Table 2. Unlike high Hg exposure from fish consumption in coastal areas, population with high Hg exposure via rice consumption is generally distributed in Hg or gold mining areas. Currently, most studies on human MeHg exposure via rice intake are concentrated in Hg-contaminated areas in China [9,18,21]. Low levels of hair THg in rice-exposed populations were found in nonpolluted areas. The average of hair THg concentration in Guizhou population is 0.46 μg/g [15]. Residents located in Hg mines showed high hair THg concentrations. The means of hair THg concentrations in Wanshan and Wuchuan Hg mines were 1.53 μg/g (0.21−12.6 μg/g) and 2.71 μg/g (1.13−4.27 μg/g), respectively [9,21]. Since rice grown in the Hg mining area can bioaccumulate MeHg, resulting in high risk of MeHg exposure in local residents.

Health effects from MeHg exposure via rice consumption

It is generally believed that about 95% of ingested MeHg can be absorbed by the body to participate in the body's reaction. MeHg can bind to the hemoglobin of red blood cells in the blood and is transported to various tissues of the body through the blood circulation [44]. Meanwhile, MeHg can bind to cysteine to form complex (MeHg−cysteine), which can cross the blood−brain barrier and the placental barrier causing damage to the brain and fetus [45]. Demethylation of MeHg *in vivo* occurs mainly in the liver and intestine [46,47]. The main route of human Hg excretion is feces and urine in the form of IHg [44].

In animal experiments, the rats feeding with rice with low MeHg dose (10 ng/g) had no observable effects on organ development [48]. The distributions of MeHg in organs of rats feeding with rice containing high MeHg dose (25 ng/g) were as follows: kidney > hair > blood > liver > brain > muscle [48,49]. The liver and kidney have positive detoxification effect on heavy metals. The portion of MeHg found in THg in the blood and brain showed relatively higher ratios than that in other organs, with averages of 89.8 ± 10.1% and 67.0 ± 16.9%, respectively [49]. Demethylation of MeHg in the intestine was the important detoxification process in the rat body [50,51]. The gut microbiota was confirmed to be a potential factor causing individual variation in MeHg absorption and potential toxicity [52,53].

In addition, exposure to MeHg can reduce antioxidant activity and damaged the nervous system in rats. The consumption of Hg-contaminated rice caused significant decreases in the antioxidant enzymatic activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and concentration of serum nitric oxide (NO) in rats [54]. GSH-Px is an important target and major cellular defense against MeHg-induced neurotoxicity [55]. Activities of GSH-Px were significantly decreased in exposed groups [48]. Low-dose MeHg exposure will stimulate acetylcholine (Ach), and long-term stimulation will result in a decline in the function of the neurotransmitter [48,54]. The expression levels of c-jun and c-fos genes in the rat brain were significantly induced by MeHg-polluted rice [56,57].

Hair MeHg levels are highly elevated at the same exposure dose for the population consuming MeHg-contaminated rice relative to fish [8]. Rice grain as the staple food does not have the beneficial nutrients such as

Table 2

Hair THg concentrations in rice Hg−exposed populations in different study areas (μg/g).

Study area	Sample size	Hg level	Polluted area or not	Reference
Guizhou, China	46	0.46	–	[15]
Gaohong, China	65	0.983	Fluorescent lamp manufacturing area	[18]
Wanshan, China	314	1.53	Hg mine	[9]
Wuchuan, China	10	2.71	Smelt workshop	[21]
Gouxi, China	13	7.55	Hg mine	[39]

n-3 fatty acids found in fish tissues, which may potentially increase the risk of MeHg-related neurodevelopmental and cardiovascular diseases [58]. The 0.14 points of per-fetus intelligence quotient (IQ) decrements and 7360 deaths from fatal heart attacks are related to MeHg exposure from Hg-containing foods in China (e.g. rice, fish, vegetables, and meat) [59]. Children in Hg mining areas with hair Hg $\geq$ 1 μg/g were 1.58 times more likely to have an IQ score <80, which is the clinical cutoff for borderline intellectual disability [9]. More researches are needed to investigate the effects of Hg exposure on neurodevelopmental, cardiovascular, and immune effects in the population via rice consumption.

Conclusion

The general population is mainly exposed to MeHg through fish consumption; recent evidence indicates that rice can bioaccumualte MeHg. Although human Hg exposures through rice consumption in most nonpolluted areas were relatively low, the high daily intake and large consumed population make it become a non-negligible pathway of human MeHg exposure. In addition, globalization has expanded the impact of rice MeHg exposure through the international rice trade. Rice does not have the beneficial nutrients such as n-3 fatty acids found in fish tissues, which may potentially increase the risk of MeHg-related diseases such as neurodevelopmental and cardiovascular diseases.

More researches are needed to evaluate human MeHg exposure via rice consumption. Currently, most of researches on human MeHg exposure via rice consumption were investigated in China, and it should expand to other Hg-polluted areas over the world. More studies are needed to reveal the mechanism of MeHg accumulation in rice because it can provide scientific advice to reduce MeHg pollution in rice. In addition, more researches are also needed to investigate the neurodevelopmental, cardiovascular, and immune effects of Hg exposure in the rice consumption population.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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