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Long-term exposure to methylmercury and its effects on hypertension in Minamata ☆, ☆☆

Takashi Yorifuji [a,*], Toshihide Tsuda [b], Saori Kashima [a], Soshi Takao [a], Masazumi Harada [c]

[a] Department of Epidemiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Okayama 700-8558, Japan
[b] Environmental Epidemiology, Okayama University Graduate School of Environmental Science, Okayama, Japan
[c] Department of Social Welfare Studies, Kumamoto Gakuen University, Kumamoto, Japan

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ABSTRACT

Recent studies suggest potential adverse effects of methylmercury exposure on cardiovascular disease, although the evidence of association with hypertension is still inconsistent. Therefore, we evaluated the effects of methylmercury exposure on hypertension in Minamata. We used data derived from the 1971 population-based survey in Minamata and neighboring communities. We also utilized data on hair mercury content of the participants (derived from a 1960 investigation). We adopted two exposure indices (residential area and hair mercury content) and two hypertension outcomes (past history of hypertension and hypertension defined by measurements in the examination). Then, we estimated the adjusted prevalence odds ratio (POR) and its confidence interval (CI) of both hypertension outcomes in relation to residential area and hair mercury content. In the Minamata area (high exposure area), 87% (833) of the eligible population (aged $\geq$10 years) participated in the 1971 investigations. In the Goshonoura area (middle exposure area) and the Ariake area (low exposure area), 93% (1450) and 77% (755), respectively, of the eligible population participated. Compared with subjects in the Ariake area, the subjects in the Minamata area manifested hypertension more frequently, and PORs observed for two hypertension outcomes were 1.6 (95% CI: 1.2–2.1) and 1.4 (95% CI: 1.1–1.9), respectively. Furthermore, dose-response trends with hair mercury content were observed for both hypertension outcomes. The present finding supports the causal relationship between methylmercury exposure and hypertension.

1. Introduction

It is well-known that acute and chronic exposure to methylmercury causes neurological signs in adults and children (USEPA, 1997). Indeed, in large-scale poisonings caused by methylmercury in Minamata and Iraq, patients manifested various neurological signs, including paresthesia, ataxia, constriction of the visual field, dysarthria and hearing difficulties (Bakir et al., 1973; Harada, 1995). More recent studies suggest that prenatal exposure to lower concentrations of methylmercury than those in Minamata and Iraq induces detrimental effects on neurologic development (Grandjean et al., 1999; Grandjean and Landrigan, 2006).

Furthermore, recent studies suggest potential adverse effects of methylmercury exposure on cardiovascular disease (Stern, 2005). Indeed, some studies demonstrated a causal association between methylmercury exposure from fish consumption and heart disease, particularly myocardial infarction (Guallar et al., 2002; Salonen et al., 2000, 1995). However, the mechanisms by which methylmercury causes cardiovascular disease are not fully understood (Virtanen et al., 2007). In particular, the evidence of an association between methylmercury exposure and hypertension is still inconsistent (Stern, 2005; Virtanen et al., 2007). The adverse effect of adult exposure on hypertension was implied by studies several decades ago (Fujino, 1977; Hunter and Russell, 1954; Tatetsu et al., 1972). Recent studies also demonstrated associations between adult and prenatal exposure to methylmercury and hypertension (Choi et al., 2009; Fillion et al., 2006; Sorensen et al., 1999). However, some other studies found no evidence of any adverse effect due to exposure (Dorea et al., 2005; Oka et al., 2002; Thurston et al., 2007).

In the present study, we used data derived from the 1971 population-based survey in Minamata and neighboring communities (Tatetsu et al., 1972; Yorifuji et al., 2008). We also used data on hair mercury content of the participants (derived from a 1960 investigation) (Doi and Matsushima, 1996; Matsushima and Mizoguchi, 1996). As described below, since residents were exposed

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* Corresponding author. Fax: +81 86 235 7178.
E-mail address: yorichan@md.okayama-u.ac.jp (T. Yorifuji).

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for more than 25 years until early 1970s, we adapted residential area as an exposure indicator in main analyses. Then we quantitatively evaluated the effects of adult and prenatal exposure to methylmercury on hypertension examined in 1971 survey.

2. Methods

2.1. Study areas and subjects

First, we introduce the history of Minamata disease briefly. Severe neurologic disorders among people living in Minamata (in the southwestern part of Kumamoto in Japan) were first officially recognized in 1956 (Fig. 1) (Harada, 1995). After the first patient was officially identified in 1956, numerous cases were reported and the first patient recognized to have the disease was identified as someone displaying the symptoms of the condition in 1953 in the initial study; subsequently this was changed and the first patient with disease was identified as having it in 1942 (Nishigaki and Harada, 1975). Methylmercury was produced as a byproduct of acetaldehyde production and had been discharged into Minamata Bay (a small part of the Shiranui Sea) from a local chemical factory. In 1958, the factory rebuilt its wastewater drainage channel, diverting wastewater directly into the Minamata River (Harada, 1995). As a result, methylmercury contamination spread throughout the entire Shiranui Sea (Ninomiya et al., 1995, 2005; Yorifuji et al. 2008). Acetaldehyde production peaked in 1960, and the methylmercury concentrations in the umbilical cords of newborns on the Coast of the Shiranui Sea corresponded with the acetaldehyde production and also peaked in 1960 (Nishigaki and Harada, 1975). Thus, the magnitude of exposure was assumed to be the highest in the early 1960s. Then, the acetaldehyde production decreased gradually and the discharge of wastewater was stopped in 1968. However, mercury content in fish in the Shiranui Sea was higher than that in Ariake Sea (Fig. 1) even in early 1970s (Fujiki and Tajima, 1973). Indeed, methylmercury concentrations in the umbilical cords from some babies born in early 1970s were still high and exceeded the value of 0.4 μg/g, which was considered to be upper limit value in Japan by Murata et al. (Harada and Yorifuji, 2009; Murata et al., 2007). Murata et al. reviewed three umbilical cord surveys targeting healthy people in Japan and estimated that the value of 0.4 μg/g was considered as upper limit value of babies in Japan (Murata et al., 2007). Although residents voluntarily and temporary stopped fishing only in small Minamata Bay in the late 1950s briefly, fishing in the Shiranui Sea had never stopped (Tsuda et al., 2009). Therefore, residents around the Shiranui Sea consumed contaminated fish for more than 10 years after the first recognition of the disease, and for more than 25 years since the first case in 1942.

In 1971 three years after the discharge of wastewater was stopped, a population-based study of neurologic signs was conducted by researchers at Kumamoto University. This was a cross-sectional study and is described in detail elsewhere (Tatetsu et al., 1972; Yorifuji et al., 2008). Thus, we describe it only briefly here. One of the present authors (M.H.) was a member of that investigation. Neurologic signs characteristic of methylmercury exposure were examined in the Minamata, Goshonoura and Ariake areas (Fig. 1). Minamata area in the study consists of three villages along Minamata Bay. Most residents had been eating contaminated fish on a daily basis. Goshonoura area is on the other side of the Shiranui Sea. Residents there also consumed contaminated fish, although the distance from the factory was about 20 km. Ariake area does not face the Shiranui Sea; it was investigated as a reference area in 1971. The combined population of the villages in each of the three areas was 1120, 1845, and 1165 people, respectively. In the present study, we excluded residents <10 years of age, because they were too young to undergo blood pressure measurement.

Furthermore, in 1960, researchers from the Kumamoto Prefecture Institute for Health Research investigated total mercury content in hair samples of 1694 residents living on the Coast of Shiranui Sea, including the Minamata and Goshonoura areas (Doi and Matsushima, 1996; Matsushima and Mizoguchi, 1996; Ninomiya et al., 2005). In sub-analyses, we also targeted 120 residents of Minamata and Goshonoura who were included in both investigations (1960 and 1971) (Yorifuji et al., 2009).

2.2. Measurement of exposure

We adopted two exposure indices: residential area, described above, and hair mercury content. As mentioned, in 1960, hair samples were collected from healthy fisherman on the Coast of the Shiranui Sea. In Minamata, the median level of mercury was 30.0 μg/g, with an interquartile range of 39.8 μg/g (Ninomiya et al., 2005). In Goshonoura, the median was 21.5 μg/g, with an interquartile range of 24.0 μg/g (Ninomiya et al., 2005). In Kumamoto City (the most distant from Minamata in Fig. 1), the median was 2.1 μg/g, with an interquartile range of 1.3 μg/g (Ninomiya et al., 2005). We have no hair mercury content information from our study area of Ariake. However, because it (like Kumamoto) is on the Ariake Sea rather than the Shiranui Sea, we assume that Ariake had a similar low exposure to methylmercury. Indeed, it was reported that mercury concentration in cats' organs on the Coast of the Ariake Sea was quite low compared to that of Minamata or other areas around Shiranui Sea in 1960 (Kitamura et al., 1960). It was also reported that, even in early 1970s, mercury content in fish in the

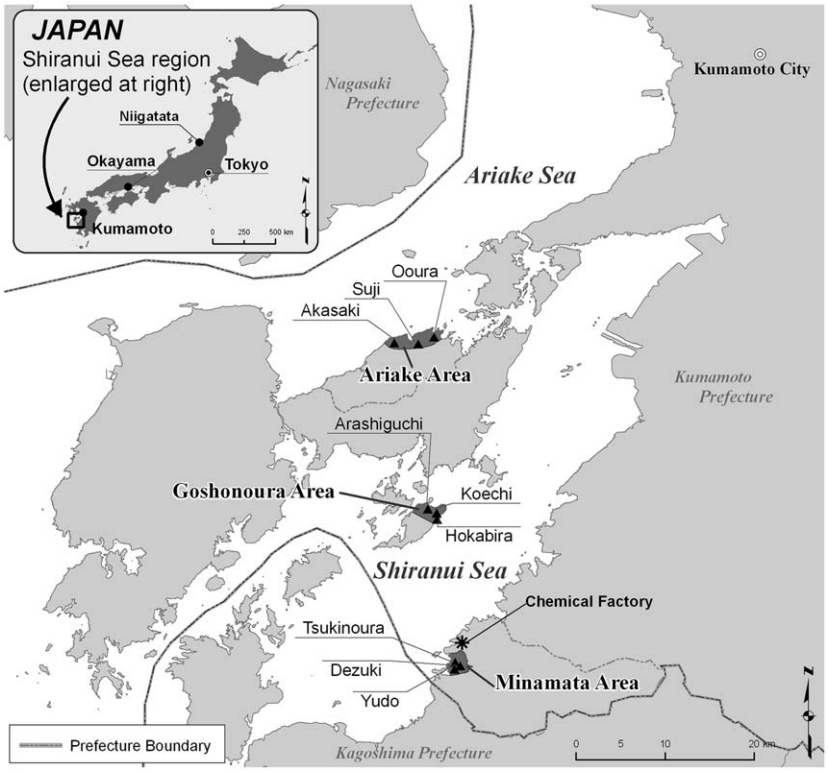

Fig. 1. . Map of the study areas.