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Original Article

Mercury Exposure in Children With Autistic Spectrum Disorder: Case-Control Study

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ABSTRACT

Although mercury has been proven to be a neurotoxicant, there is a lack of data to evaluate the causal relationship between mercury and autism. We aim to see if there is increased mercury exposure in children with autistic spectrum disorder. We performed a cross-sectional cohort study over a 5-month period in 2000 to compare the hair and blood mercury levels of children with autistic spectrum disorder (n = 82; mean age 7.2 years) and a control group of normal children (n = 55; mean age 7.8 years). There was no difference in the mean mercury levels. The mean blood mercury levels of the autistic and control groups were 19.53 and 17.68 nmol/L, respectively (P = .15), and the mean hair mercury levels of the autistic and control groups were 2.26 and 2.07 ppm, respectively (P = .79). Thus, the results from our cohort study with similar environmental mercury exposure indicate that there is no causal relationship between mercury as an environmental neurotoxin and autism. (*J Child Neurol* 2004;19:431–434).

For more than 3000 years, mercury and its derivatives were widely used as antiseptics, antiparasitics, antisyphilitics, dental amalgams, and medical, cultural, and other folk remedies. Following its increasing industrial application, the environmental mercury level has been estimated to have a threefold increase in the past century.[1] The two disasters of mercury poisoning that occurred in Minamata Bay, Japan, in 1950 to 1960 and in Iraq in 1971 to 1972 related to consumption of mercury-contaminated fish and mercury-containing fungicide in seed grain, respectively, confirmed mercury as a neurotoxicant and provided important information for understanding mercury poisoning.[2]

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At high concentrations, mercury could lead to hepatic, renal, and neurologic damage.[2] However, there is still limited understanding of the effects of low-dose chronic mercury exposure.[3]

Autistic spectrum disorder, or autism, is a common neurodevelopmental disorder in childhood, affecting at least 4.8 per 10,000 children.[4] Recent studies reported 1 in every 1000 children or even a higher prevalence if the entire autistic spectrum disorder was taken into consideration.[5,6] The report of the Department of Developmental Services of California has been widely quoted as evidence for an epidemic of autism.[7] A recent review of 23 epidemiologic surveys of autism (1966–1998) revealed a significant increase in the prevalence rates of autism. There was a recent debate on whether there is a true epidemic of autism or whether this secular increase in the rates of autism might be due to changes in case definition, improved recognition, and specific methodologic limitations.[8,9]

Because chronic low-dose mercury exposure has already been reported to have harmful effects on neurodevelopment, it could also be a potential factor accounting for the increasing prevalence rate of autism. To date, there are no scientific data on the relationship between mercury exposure and autism. We therefore determined the blood and hair mercury levels of children with autistic spectrum disorder and compared their values with those of normal children.

METHODS

Study Participants

A cross-sectional study was performed from April to September 2000. Altogether, 82 children with autistic spectrum disorder and 55 children with normal development were recruited. Written consent was obtained from their parents after explanations of the details of the study. A questionnaire on sociodemographic data, dietary habits, and other risk factors for environmental mercury exposure was completed by the parents. The study was approved by the Ethical Committee of the Faculty of Medicine, The University of Hong Kong.

The autistic group (n = 82) included all autistic children actively followed up during the study period in the Duchess of Kent Children's Habilitation Institute, a major developmental assessment and training center in Hong Kong. All autistic children were assessed by the second author. The diagnosis of autistic spectrum disorder was made only if they fulfilled the *Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)* diagnostic criteria for autism and undergone a structured interview using the Autism Diagnostic Interview-Revised. The Autism Diagnostic Interview-Revised is a structured parent interview in the fields of social relatedness, communication, and ritualistic or perseverative behavior. All children with autistic spectrum disorder had mild to moderate mental retardation.

The control group (n = 55) consisted of normal children who had mild viral illness and were admitted to the pediatric ward of Queen Mary Hospital, the major teaching hospital of the University of Hong Kong, during the same period.

Mercury Analysis

Hair and blood samples were collected simultaneously and were sent for mercury analysis. Hair samples were taken in a standardized fashion. The first 1.5 inches (from the root) of hair was cut from the scalp, and 350 mg of hair was collected from each subject. The hair samples were then sent to the Mineralysis Laboratory in Texas for mercury analysis. Each hair sample was washed with distilled and deionized water to remove any adsorbed or external contaminants and was then dissolved in ultrapure trace metal grade HNO_3 and digested at 100°C for 15 minutes in temperature-controlled heating blocks within an acid digestion fume hood. The quantitative analysis of mercury was performed using flow-injection mercury system–atomic absorption spectroscopy. Quality control was maintained using certified aqueous standards, homogeneous in-house sample controls, reagent blanks, and reference materials from the US Institute of Standards and Technology. Calibration checks were undertaken following every tenth process.

Blood samples were collected by venipuncture and analyzed at the Clinical Biochemistry Laboratory of Queen Mary Hospital. The total mercury level in the whole blood was determined using a Varian AA 40 atomic absorption spectrometer coupled with a vapor generation accessory by the cold vapor method. Quality control was maintained by internal and external QA assessment schemes.

Statistical Analysis

Analyses were conducted using SAS software, version 6.12 (Cary, NC). Student's t-test was used to compare the age, mean blood mercury level, and mean hair mercury level between the autistic and the normal group. Chi-square test was used to test the sex ratio and social class between the autistic and the normal group. A significance level of $P < .05$ was used for all analyses.

RESULTS

Subject Characteristics

One hundred and thirty-seven Chinese children were recruited (119 boys, 18 girls). The mean age was 7.4 ± 0.3 years (range 4–11 years). The cohort consisted of 82 children with autistic spectrum disorder and 55 children with normal development.

In the group with autistic spectrum disorder, 73 were male and 9 were female. The mean age was 7.2 ± 0.2 years. In the control group, 46 were male and 9 were female. The mean age was 7.8 ± 0.4 years. There was no significant difference in age (P = .28), sex (P = .44), or social class (P = .67) between children in the autistic spectrum disorder and in the control group.

Mercury Level

The mean hair mercury level of autistic children was 2.26 ± 0.21 ppm. The level in the control group was 2.07 ± 0.58 ppm. There was no statistically significant difference between the two groups (P = .79). The mean blood mercury level of the autistic children was 19.53 ± 5.65 nmol/L, whereas the control group level was 17.68 ± 2.48 nmol/L (P = .15) (Table 1).

DISCUSSION

This is the first control study to investigate mercury exposure in children with autistic spectrum disorder. According to a local unpublished pilot study performed on 20 autistic children at the Duchess of Kent Children's Habilitation

Table 1. Mercury Levels in Children With Autistic Spectrum Disorder and a Control Group

	Autistic Spectrum Disorder (n = *82*)	*Control (Normal Development)* (n = *55*)	P *Value*
Age (yr) (mean ± SD)	7.2 ± 0.2	7.8 ± 0.4	NS
Sex			
Male	73	46	NS
Female	9	9	NS
Blood mercury (nmol/L) (mean ± SD)	19.53 ± 5.65	17.68 ± 2.48	NS
Hair mercury (ppm) (mean ± SD)	2.26 ± 0.21	2.07 ± 0.58	NS

NS = not significant.

Institute from January to February 2000, their blood mercury levels were significantly elevated. We therefore performed a case-control study to delineate the problem and investigate environmental mercury exposure in children with autistic spectrum disorder and normal children.

The pathogenesis of autism is unknown. There are still gaps in our knowledge about the mechanisms leading to such a heterogeneous spectrum of disorder with "autistic" traits as the core neurobehavioral symptomatology. The scientific literature supports a genetic predisposition to autistic disorder. A recent genome screen for autism has demonstrated strong linkage to chromosomes 2q, 7q, 15q, and 16p.[10,11] As many as 10 genes can interact to cause the disorder.[12] In view of the possible multifactorial cause, autistic spectrum disorder can occur as a result of interaction between environmental neurotoxicant exposure and the brain at a critical period of neurodevelopment in a child with genetic predisposition.

Environmental exposure to neurotoxicants, especially mercury, has drawn much attention from professionals and the public in the past decade. Prenatal exposure to methylmercury from contaminated seafood was associated with an increased risk of neurodevelopmental deficit.[13] In the Danish study of children of the Faroe Islands in the north Atlantic, neuropsychological dysfunctions were found at low-level mercury exposures. This longitudinal study uncovered deficits in language, memory, and attentional neuropsychological measures among children evaluated at 7 years associated with maternal exposure to mercury during pregnancy.[14] In 1997, the US Environmental Protection Agency proposed reducing the safe level for mercury exposure to 0.1 μg/kg/day,[15] whereas the previous standard of the US Food and Drug Administration was five times higher. This stricter safety level was endorsed by the panel of the National Academy of Sciences in 2000.[16] Other studies, such as those in the Republic of Seychelles involving a longitudinal cohort study of the effects of prenatal and postnatal mercury exposure from fish consumption on neurodevelopment, are ongoing, and more sensitive neuropsychological tests are used.[17]

The issue of whether the increased prevalence rate of autism could be related to the increasing environmental pollution and poisoning in the past decades has raised much concern, leading to impassioned discussions. Some studies have suggested a relationship between lead poisoning and attention-deficit hyperactivity disorder (ADHD),[18,19] and one small-scale study also showed elevated blood lead levels in children with autism.[20] However, to date, there are no scientific data on the relationship between mercury exposure and autism. Recent reports on iatrogenic mercury exposure related to thimerosal-containing vaccines have raised much concern about the neurotoxicity of mercury poisoning and its potential effects on neurodevelopment and pervasive developmental disorders.[1,21] The issue was further complicated by the promotion of chelation therapy and mercury detoxification by some investigators for treatment of autistic children with high tissue mercury levels.[22,23] Hence, a well-designed control study would be necessary to delineate the issue and alleviate the worrying of parents of autistic children.

In our study, the hair and blood mercury levels of both autistic and normal children in Hong Kong were elevated.[24,25] The differences in hair and blood mercury level between the autistic and control group were not statistically significant. The detected elevated tissue mercury level of autistic children reflected an environmental mercury exposure that also occurred in children with normal development. Some have proclaimed that chelating therapy for suspected mercury poisoning cures those autistic children with a higher mercury level. Our pilot study demonstrates that this is not based on hard-core evidence. A more logical step is to identify the source of mercury exposure in the child population and consider prevention and control of environmental pollution.

Our study is one of the few to investigate the relationship between autistic spectrum disorder and mercury exposure in children. We did not detect any significant difference in tissue mercury levels between autistic children and the control group. However, this study is limited by the sample size and the culture because Hong Kong Chinese are famous for eating seafood; therefore, the source of mercury in seafood might be higher. Further large-scale, multicenter, control studies in autistic patients of different cultures with different eating habits are worthwhile to delineate this issue.

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