SHORT REPORT

Chinese herbal medicine, sibship, and blood lead in children

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Abstract
***Objectives*—Risk factors for increased blood lead concentration (BPb) has been investigated. However, the effect of sibship and Chinese herbal medicine on BPb has not been systematically studied. In this study BPb data from voluntary testing was used to determine if Chinese herbal medicine and sibship were associated with BPb.**
***Methods*—319 children aged 1–7 were tested for BPb. Meanwhile, parents were interviewed to obtain information including consumption of Chinese herbal medicine, living environment, lifestyle, and sibship of the children tested.**
***Results*—The mean (SD) BPb of 319 preschool children was 4.4 (2.4) µg/dl. The consumption of Ba-baw-san (a Chinese herbal medicine) was significantly associated with increased BPb in children (p=0.038). Further multivariate regression analysis of BPb in 50 pairs of siblings showed the factors of being brothers explained 75% of variation for BPb, and being sisters and brother-sister explained 51% and 41% of variation respectively.**
***Conclusion*—Chinese herbal medicine and children's play patterns within the family expressed in different types of sibship are the main determinants of low concentrations of BPb in preschool children of Taiwan.**

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Keywords: Chinese herbal medicine; sibship; blood lead

Previous studies have indicated that there is a dose-response relation between children's cognitive development and blood lead concentrations (BPb).[1–5] In the United States, the Center for Disease Control and Prevention has lowered the acceptable BPb for children from 25 µg/dl to 10 µg/dl and revised the guidelines for screening and management of increased BPb. The guidelines call for universal screening of children <6 years of age for increased BPb unless the community does not have a childhood lead poisoning problem.[6] Similar guidelines were adopted by the American Academy of Pediatrics in 1993.[7]

Children are exposed to lead from different sources and through different pathways. In Taiwan, children's lead exposure has been reported to be associated with environmental pollution from factories that use lead in the neighbourhood[8–10] and from leaded petrolium.[11] Also, Chinese herbal medicine was responsible for children's lead poisoning in some case reports.[12–13] As there is no routine lead screening for children in Taiwan, the distribution of BPb is not clear.

Having a sibling who had an increased BPb concentration was rated as one of the primary risk factors by United States paediatricians in screening their patients.[14] Researchers indicated that having a sibling, housemate, or playmate who was followed up or treated for lead poisoning was significantly associated with an increased adjusted odds ratio for increased BPb in both urban[15] and rural[16] settings. In a pedigree study of subjects aged 6–91, there was a 50% correlation of BPb concentrations for siblings living together, and only 10% in those living apart.[17] However, the association of children's BPb and sibship effects has not been thoroughly studied.

In this study, we reported the results of a voluntary BPb test for children in the metropolitan Taipei area sponsored by the Department of Health of Taiwan. The source and pathway of lead exposure in children and the correlation of BPb between siblings of different combinations (brothers, sisters, and brother-sister) were also investigated.

Materials and methods

In mid-August 1995, the Consumer Protection Foundation in Taiwan reported that some sweet wrappers might contain high concentrations of lead. Parents who lived in the metropolitan Taipei area (including Taipei City, Taipei County, and Tau-Yuan County) were advised to bring their children to the Center for the Research of Environmental and Occupational Diseases for free BPb tests sponsored by the Department of Health of Taiwan.[18]

A total of 319 children aged 1–7 were tested and their parents were interviewed to obtain information on children's age, sex, diet, sweet

Table 1 Demographic characteristics of study subjects

Variables	*Boys (n=180)*	*Girls (n=139)*
Blood lead (μg/dl)*	4.51 (2.82)	4.16 (2.96)
Age (y)*	4.37 (1.45)	4.42 (1.49)
Height (cm)*	104.58 (11.52)	103.94 (11.84)
Weight (kg)*	17.12 (4.39)	16.87 (3.94)
BMI (kg/m^2)*	15.79 (3.62)	15.35 (3.56)
Drinks milk regularly (%)	69.8	77.0
Chinese herbal medicine (%)	41.3	41.0

*Mean (SD).

Table 2 Blood lead concentrations by sex, age, diet, and living environment in children

Variables	*n*	*Mean (SD)*
Sex:		
Boy	180	4.51 (2.93)
Girl	139	4.16 (2.96)
Age (y):		
1	7	3.53 (2.41)
2	37	3.71 (3.50)
3	48	4.12 (2.73)
4	75	4.39 (2.32)
5	81	4.54 (2.78)
6	58	4.72 (3.15)
7	16	3.42 (2.66)
Have taken Chinese herbal medicine:		
Yes	130	4.85 (2.91)
No	184	4.02 (2.83)*
Have taken Ba-baw-san:		
Yes	66	4.96 (2.71)
No	233	4.13 (2.83)*
Drinks milk regularly:		
Yes	282	4.41 (2.93)
No	32	3.83 (2.48)
Drinks tap water:		
Yes	303	4.41 (2.90)
No†	12	3.11 (1.99)*
Living environment:		
House newly painted:‡		
Yes	114	4.11 (3.02)
No	196	4.48 (2.74)
Peeling paint:		
Yes	138	4.27 (2.50)
No	169	4.48 (3.17)
Lives on the first floor:		
Yes	270	4.50 (2.71)
No	45	4.31 (2.94)
Kindred with lead poisoning:		
Yes	8	5.95 (1.11)
No	307	4.31 (2.90)**

*0.01<p<0.05; **p<0.01.
†No tap water, only well water , spring water, or others.
‡Including children's house, babysitter's house, and nursery school.

Table 3 Demographic characteristics of 50 sibling pairs

Variables	*Elder sibling*	*Younger sibling*
BPb (μg/dl)†	3.93 (2.24)	3.96 (2.20)
Male (%)	66.0	52.0
Age (y)†	5.24 (1.16)	2.95 (1.58)*
Height (cm)†	112.4 (19.8)	94.7 (11.0)*
Weight (kg)†	15.7 (4.5)	14.3 (3.4)*
Body mass index(kg/m^2)†	15.7 (2.4)	15.7 (2.8)
Drinking milk every day (%)	62.0	74.0
Chinese herbal medicine (%)	36.0	28.0

*p<0.05, Wilcoxon rank sum test.
†Mean (SD).

consumption, milk consumption, drinking water, and medical history including consumption of Chinese herbal medicine. Information about their living environment was also obtained, including whether they lived in a newly painted house and the distance between their house and main streets. Information on family members engaged in lead related industries was also inquired.

Whole blood (2 ml) was drawn intravenously into a heparinised tube. The specimens were stored in a 4°C refrigerator until analysis. Blood lead concentration was measured with a graphite furnace atomic absorption spectrophotometer in our laboratory within one week.[19] Our laboratory has joined the Center for Disease Control and Prevention lead proficiency programme and maintained good quality control since 1986.

As this was a voluntary testing programme, many parents brought in not only one child but all their children to the test. Among the 319 children tested, there were 58 sets of siblings (including 54 sets of twos, two sets of threes, and two sets of twins) which provide a unique chance for the researchers to investigate the relation of BPb and sibship. Fifty pairs of siblings were chosen for further analysis after one pair of children with increased BPb values (>10 μg/dl) and seven pairs of siblings with different histories of taking Ba-baw-san were excluded. Among the seven pairs with discordant histories, there was one pair of brothers, one pair of sisters, and five pairs of cross sex siblings. In sibling sets of threes, the two younger ones were chosen. The association of BPb concentrations and sibship was explored in this study.

Data analyses were performed with SAS package software.[20] Unpaired *t* test, analysis of variance (ANOVA), non-parametric tests, and multiple regression modelling were performed to explore the risk factors of BPb. Under the multiple regression analysis, BPb was modelled as a function of various risk factors, including sibling's age, sex, milk consumption, various living environments, and lifestyle.

Results

The mean (SD) BPb of 319 children was 4.4 (2.4) μg/dl. Eight children (2.5% of the children tested, four boys and four girls) had BPb >10 μg/dl (11.4–20.8 μg/dl). Among the eight children with increased BPb, six of them had been taking Chinese herbal medicine (three of them taking Ba-baw-san). Two of these eight children were brothers, a boy and a girl had same sex siblings with lower BPbs, and the other four children did not have any sibling participating in the lead test.

Blood lead, age, height, weight, body mass index (BMI), drinking milk, and taking Chinese herbal medicine were not significantly different between sexes (p>0.05, unpaired *t* test, table 1. Thirty five per cent of the paternal occupations were business, and about 30% were government employees, whereas 40.3% of the maternal occupations were housekeeping and 24.7% were business.

The univariate analysis showed that BPbs were significantly higher for children who had ever taken Chinese herbal medicine, drank tap water, or had kindred diagnosed as lead poisoned (p<0.05, unpaired *t* test, table 2). There were no significant associations between BPb and other factors including sex, age, consistently drinking milk, peeling paint in their living environment, and living on the first floor (table 2). Because the only Chinese herbal medicine that most children had taken was Ba-baw-san, further analysis was focused on the association between taking Ba-baw-san and BPb. Those who had ever taken Ba-baw-san, had a higher mean BPb than those who had

Table 4 Relation of blood lead concentrations (BPb) between siblings†

Blood lead concentrations	*Pairs (n)*	*Age difference*	*BPb mean (SD)*	*BPb difference between siblings‡*	R^2
Brother-brother	18	2.3 (1.1)	4.1 (2.1)	0.8 (0.8)	0.75
Sister-sister	10	2.3 (1.1)	4.3 (2.1)	1.5 (1.5)	0.51
Cross sex	22	2.3 (0.7)	3.7 (2.3)	1.6 (1.2)*	0.41
Younger-elder sibling	50	2.3 (1.0)	3.9 (2.2)	1.3 (1.2)	0.48

*p<0.05, Wilcoxon rank sum test, *v* BPb differences among siblings.
†Adjusted for administration of Ba-baw-san.
‡There was a significant difference among three categories (p<0.05, Kruskal-Wallis test).
Values are mean (SD).

never taken it (4.96 (2.71) µg/dl *v* 4.13 (2.83) µg/dl, p<0.05). Among children who had taken Ba-baw-san (20.75% of all children tested) the mean BPb of boys was significantly higher than that of girls (5.63 (2.77) µg/dl *v* 4.21 (2.46) µg/dl, p<0.05). The mean BPb in those who had taken Ba-baw-san reached a peak at the age of 2–3. However, age was not significantly associated with BPb in children who had never taken Ba-baw-san. In further multiple regression analysis, only the factor of taking Ba-baw-san was positively associated with BPb (p=0.038).

Fifty pairs of siblings were chosen for further analysis. Table 3 shows the demographic characteristics of the 50 sibling pairs. The 50 pairs of siblings were further divided into three categories: brothers (18 pairs), sisters (10 pairs), and cross sex siblings (22 pairs). Difference in BPb between brothers was 0.8 µg/dl; it was 1.5 µg/dl between sisters and 1.6 µg/dl between cross sex siblings. Difference in BPb between brothers was significantly lower than that between cross sex siblings, and lower than that between sisters although not significantly. Regression analysis showed that the factor of being siblings could explain 75%, 51%, 41% of BPb variation in brothers, sisters, and cross sex siblings, respectively. Age difference and mean BPb were not significantly different among these three categories (p>0.05, table 4).

Discussion

Data for BPb distribution in children are limited in Taiwan. In this study, the mean BPb of 319 children was 4.4 (2.4) µg/dl. The BPb might either underestimate the true value because the parents had high socioeconomic status, or overestimate because the children were brought in under the suspicion of increased lead absorption from sweet wrappers. Although the direction and magnitude of possible bias in this study could not be determined, the mean BPb was below the guideline of 10 µg/dl. With similar diet and cultural background, the BPb in Taiwanese children is much lower than that in children of China (mean BPb 21.8–67.9 µg/dl in different areas).[21] The introduction of unleaded petrolium since 1984 in Taiwan could be the main reason for the lower BPb in Taiwanese children.

The episode of lead contaminated sweets was later proved to be an overstatement by the media,[18] the low dose of lead in sweets could not have caused any adverse health effect, and sweet consumption was not related to increased BPb in children. However, the popular use of Chinese herbal medicine containing lead in Taiwanese families calls for more public health attention. The use of Chinese herbal medicine and lead poisoning has been reported in children and adults in Taiwan, China, and the United States.[12–13 22–24] In this study, Chinese herbal medicine was the main source of exposure to lead for children with increased BPb in Taiwan. An amazingly large proportion of children enrolled in this study had been taking Chinese herbal medicine (41.3% of boys and 41.0% of girls), especially Ba-baw-san. Ba-baw-san (Ba-baw-neu-hwang-san) has been used for treating infants and young children since China's Song dynasty (960–1279). It is used by many parents to detoxify infant's "fetus poisoning", to treat colic pain, or to pacify young children. The ingredients of many secret recipes varied with different amounts of heavy metals including chromium, manganese, mercury, arsenic, and lead. The content of lead in Ba-baw-san ranged from 0.7 to 7.12 µg/g.[12] Our study showed that Ba-baw-san was significantly associated with BPb (p=0.038). Moreover, BPb reached a peak at the age of 2–3 with Ba-baw-san, then gradually declined with age. In this study, boys who had ever taken Ba-baw-san had a significantly higher mean BPb than girls. It is possible that boys had taken higher doses of Ba-baw-san than girls because they were worse tempered or received more attention in Chinese families.

In tracing children's environmental exposure to lead, play patterns and playtime activity may be important. A previous study of exposed children in a kindergarten near a battery recycling plant in Taiwan showed that boys had a significantly higher BPb than girls. The authors suggested that boys were more active so inhaled more air lead, and spent more time outdoors so ingested more lead contaminated soil.[9] In this study of environmentally unexposed children, BPb was higher in boys than girls but not significantly. However, the BPb differences between brothers, sisters, and cross sex siblings probably provided another insight for the association of BPb and children's play patterns.

There is a cross cultural similarity of boys being involved in more strenuous games and athletic competitions.[25] Observation by behaviour scientists of sibship and play patterns also suggests that brothers interact differently from sisters and cross sex sibling sets.[26] A 50% correlation for BPb in siblings aged 6–91 living together was reported in a previous pedigree study.[17] In our study, the overall explainable variation of BPb between siblings was 48% after excluding seven pairs of siblings with different histories of taking Ba-baw-san (table 4). Using the explainable proportion of variations of BPbs for cross sex siblings as baseline, common heredity and common environment can account for up to 41% of variation in BPb. The 51% of total variation among sisters and 75% among brothers can probably be explained by the presence of same sex sibship effects.

We suggest that one cultural factor—Ba-baw-san—and one universal factor—sibling's play pattern—help to predict low concentrations of BPb in children. In tracing the source of exposure to lead in oriental children, the use of Chinese herbal medicine is critical. Furthermore, when one of the children showed increased BPb, all other children within the family should be screened for a similar problem, especially siblings of the same sex; and the play patterns between siblings as well as having a sibling with increased BPb, should be considered as a fisk factor for high BPb.

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