Association between Chronic Arsenic Exposure and Children’s Intelligence in Thailand

Unchalee Siripitayakunkit, Pongsakdi Visudhiphan, Mandhana Pradipasen, Thavatchai Vorapongsathron

ABSTRACT

Previous studies have reported high arsenic level in hair of children at Ronpiboon subdistrict. It is possible that the accumulation of arsenic in their bodies may adversely affect intelligence. This study aims to explore the relationship between arsenic level in hair and intelligence of children. We measured the arsenic level in hair using atomic absorption spectrophotometry method as the indicator of chronic arsenic exposure and IQ with Wechsler Intelligence Scale Test for Children. Potential confounders were collected at the same time period of this cross-sectional study between 16 January and 5 March, 1995. To explore the association, multiple classification analysis was conducted with data from 529 children aged 6-9 years who had lived in Ronpiboon district since birth. This study found an association between arsenic hair levels and children’s intelligence. After adjusting for confounders, we observed a statistically significant relationship that arsenic could explain 14% of variance in children's IQ. This result revealed that chronic arsenic exposure as shown by hair samples was related to retardation of intelligence in children. Prevention of further arsenic exposure and health status monitoring of children with arsenic accumulation should be implemented.

Keywords: association, arsenic exposure, arsenic level in hair, IQ, WISC, AAS
INTRODUCTION

Arsenic in water supplies has occasionally caused poisoning, usually of a chronic rather than acute nature (Ferguson and Gavis, 1972). Chronic environmental exposure to well water naturally high in arsenic has been described in Chile, Taiwan, Japan, and other parts of the world, including instances where keratosis, and possibly skin cancer, have resulted from such exposures (Armstrong et al., 1984). In Thailand, environmental arsenic exposure has received attention since 1987 because of skin manifestations or "Black Fever" resulting from ingestion of water containing arsenic (Division of Environmental Health, 1992; Choprapanwan, 1994). Most of the inhabitants of Ronpiboon subdistrict prefer the daily drinking and use of well-water which has been contaminated with arsenic for a long time. They have habitually ingested this well-water for drinking and cooking because it is sweet, delicious and full (Ajimangkul, 1992; Division of Environmental Health, 1992; Choprapanwan, 1994). Chronic arsenic poisoning will increase in severity day after day unless inhabitants stop ingesting well-water and the drinking water supply is made safe for them. Neither the routine monitoring of arsenic contamination of well-water nor the monitoring of public drinking water for safety is presently mandated in Ronpiboon subdistrict. The population living in this area is still at risk of gradual chronic arsenic exposure.

Examinations of skin lesions from chronic arsenic poisoning in October 1987 found that children aged less than 10 years had proportionally more severe skin lesions than other age groups. Nevertheless, children aged 12–15 years (44%) had high arsenic levels in their hair and in their nails (78%) (Piamponsant and Udornmitikul, 1989; Choprapanwan, 1994). A recent report indicated 89.8% of children aged 0–9 years were found with an arsenic level of ≥0.2 ppm in their hair (Rodklai, 1994). Many children had arsenic accumulated in their bodies though they had no skin changes. What are the health effects of chronic arsenic poisoning to these children? Is it possible that the high arsenic concentrations in their bodies will affect intellectual development? This question is interesting, yet there is no clear answer. Prior to the study, the pilot results showed that eight pupils who had accumulated high arsenic levels in their hair (>1 μg/g) had IQs between 68 and 103, and two of them were classified as mental defective. The other four pupils with normal hair arsenic levels had IQs between 83 and 122, two of them had above average intelligence. The results were interesting and suggested a further need to explore the effect of chronic arsenic exposure on the development of intelligence in young children. The children in Ronpiboon subdistrict constitute a critical group for chronic low-level arsenic exposure. It is worthwhile to undertake epidemiological investigation to determine the effect of arsenic exposure in this child group, in order to obtain information on the possible effect on the intelligence of children. The present study aimed to test the association between chronic arsenic exposure, indicated by the arsenic levels in hair, and children's intelligence among children living in Ronpiboon district since birth. It is a pioneer study conducted in humans, to try to determine the exposure factor related to the developmental defect of children with high arsenic concentrations in their hair.

METHODOLOGY

Study Population

The children who were born between 1986 and 1989 in Ronpiboon and Soa Thong subdistricts were the study population. To prevent a distorted association of results, the following criteria were employed: (1) the subjects must have lived in the study area since birth; (2) the subjects' parents must be a married couple, live together and look after the children; (3) the subjects were six to nine years old at the time of the IQ test. The subjects' selection was done using simple random sampling. We selected fifteen schools from 21 schools (71.4%) and selected 529 subjects from 838 children who met the criteria (63.1%).
Data Collection

Data were collected between 16 January and 5 March, 1995. The collection of data was done for two days in each school as follows: On the first day: (1) Each subject was interviewed using the child interview form. This form was constructed to collect variables: gender, parent arguing, child rearing and food intake. (2) The subject was measured for visual acuity and hearing with Snellen’s chart and Impact Audiometer Model 1001, respectively. (3) Child’s hair was cut approximately 2–3 cm from the scalp and about 1 g of each. (4) Then, each subject got the father’s questionnaire for completion by his father at home. The questionnaire was developed to assess father’s variables: education, history of slow learning, occupation and income. On the second day: (1) We received the fathers’ questionnaire from the subjects. (2) Each subject was administered with the Wechsler Intelligence Scale Test for Children (WISC) (Wechsler, 1949) for IQ determination by the psychologist. (3) Subjects’ mothers were interviewed for data according to the maternal interview form. This form was constructed to collect variables: prenatal factors, perinatal factors, postnatal factors, birth order, birth weight, breast feeding, illness history, food intake, family size, child rearing, mother’s education, occupation, and income. Then, they were tested for intelligence with the Progressive Matrices slides in groups of 10–15 persons.

Arsenic Analysis

The hair samples were sent to the Faculty of Pharmaceutical Science, Prince of Songkla University for arsenic analysis with atomic absorption spectrophotometry (AAS) method using a GBC 906 automatic multi-element atomic absorption spectrophotometer with the GBC HG 3000 hydride generator (Chapelle and Danby, 1990).

Statistical Analysis

Descriptive statistics of frequency and percent distribution were calculated to depict basic characteristics of the sample children as well as for arsenic level in hair and IQ. The chi-square test was performed to examine the difference of potential confounders distributed among subjects. We explained the association between arsenic level in hair and intelligence of children by simultaneously adjusting for confounders in multiple classification analysis. The data was analysed by the statistical package of SPSS/PC+ version 4 (Norusis, 1990).

RESULTS

Characteristics of the Subjects

The total study subjects numbered 529 persons: 353 from Ronpiboob subdistrict and 176 from Soa Thong subdistrict. The subjects consisted of children from kindergarten, grades I and II, 30.8%, 36.5%, 32.7%, respectively. The male to female ratio was 1.08:1. The percentage of children of the first and the second birth order was 35.2% and 28.5%, respectively. Eighty-two percent of the subjects were from families of 3 to 6 persons. Half of the subjects were from low income families (≤ 5,000 baht/month).

Distribution of Arsenic Level in Hair and IQ

The mean hair arsenic concentration for all subjects was 3.52 μg/g (SD = 3.58), the median hair arsenic was 2.42 μg/g. The range of arsenic levels in hair was 0.48 to 26.94 μg/g. Around half of the children (55.4%) had arsenic levels between 1.01 and 3 μg/g. Only 44 of 529 (8.3%) children had normal arsenic levels in hair (≤1 μg/g) as shown in Table 1. The mean IQ of the study subjects was 90.44 points. The mean of Verbal IQ, Performance IQ, and each WISC subtest scores are presented in Table 2.
TABLE 1

Number and percentage of arsenic levels in hair of children aged 6-9 years in Rongpiboon district, 1995

<table>
<thead>
<tr>
<th>Arsenic level (µg/g)</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1</td>
<td>44</td>
<td>8.3</td>
</tr>
<tr>
<td>1.01-2</td>
<td>146</td>
<td>27.6</td>
</tr>
<tr>
<td>2.01-3</td>
<td>147</td>
<td>27.8</td>
</tr>
<tr>
<td>3.01-4</td>
<td>60</td>
<td>11.3</td>
</tr>
<tr>
<td>4.01-5</td>
<td>37</td>
<td>7.0</td>
</tr>
<tr>
<td>5.01-10</td>
<td>71</td>
<td>13.4</td>
</tr>
<tr>
<td>&gt;10</td>
<td>24</td>
<td>4.6</td>
</tr>
<tr>
<td>Total</td>
<td>529</td>
<td>100.0</td>
</tr>
</tbody>
</table>

TABLE 2

Mean scaled score of WISC subtests and IQ of children aged 6-9 years, Rongpiboon district, Nakorn Si Thammarat province, 1995

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information</td>
<td>8.42</td>
<td>2.71</td>
<td>3-18</td>
</tr>
<tr>
<td>Comprehension</td>
<td>8.02</td>
<td>2.55</td>
<td>3-18</td>
</tr>
<tr>
<td>Arithmetic</td>
<td>10.51</td>
<td>2.89</td>
<td>3-20</td>
</tr>
<tr>
<td>Similarities</td>
<td>8.74</td>
<td>2.85</td>
<td>2-18</td>
</tr>
<tr>
<td>Digit Span</td>
<td>10.27</td>
<td>3.10</td>
<td>2-20</td>
</tr>
<tr>
<td>Picture Completion</td>
<td>7.40</td>
<td>2.42</td>
<td>3-18</td>
</tr>
<tr>
<td>Picture Arrangement</td>
<td>7.36</td>
<td>2.38</td>
<td>2-16</td>
</tr>
<tr>
<td>Block Design</td>
<td>8.98</td>
<td>2.31</td>
<td>2-18</td>
</tr>
<tr>
<td>Object Assembly</td>
<td>6.96</td>
<td>2.31</td>
<td>1-16</td>
</tr>
<tr>
<td>Coding</td>
<td>10.30</td>
<td>2.84</td>
<td>4-19</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>94.70</td>
<td>11.94</td>
<td>63-130</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>87.47</td>
<td>11.67</td>
<td>55-128</td>
</tr>
<tr>
<td>IQ</td>
<td>90.44</td>
<td>11.45</td>
<td>54-123</td>
</tr>
</tbody>
</table>

Most of the children's IQs were classified in the average and the dull normal groups at 45.7% and 31.6%, respectively. Around half of children (48.4%) had below average IQ with 13.8% and 3%, respectively, in the borderline and mental defective groups as shown in Figure 1. The lowest IQ of total subjects was 54, the highest was 123 and no subject scored at the very superior level.

Fig. 1. Level and percentage of IQ score of children aged 6-9 years, Rongpiboon district, Nakorn Si Thammarat province, 1995.
The findings after controlling for other risk factors showed a significant inverse relationship between arsenic levels and IQ \( (p=0.002) \). Arsenic levels could explain 14% of the variation in IQ. Other variables were significant explanatory variables of IQ; namely, maternal intelligence, occupation of father, child's age \( (p \leq 0.002) \), and family income \( (p=0.06) \).

The brain growth spurt runs from mid-pregnancy to about 3 to 4 years in humans. This period is a focus of early central nervous system (CNS) development, it is characterized by gial proliferation, and subsequently myelination. Exposure to adverse environmental circumstances and abnormal hormonal influences is dangerous at this time. It can lead to permanent impairment or alteration of CNS function that cannot be reversed (Brook, 1982; Meyer-Bahlburg, 1978). In humans, effects of metallic compounds on the developing CNS indicate that arsenic should have an adverse effect (Nordberg, 1988). The children living in the arsenic contamination area had been exposed continuously to low-dose arsenic since conception. Arsenic accumulation can be detected in hair which reflects recent chronic arsenic exposure. These children who had high arsenic concentrations in hair and lower IQ development suggested that chronic low-dose arsenic exposure might adversely affect the CNS.

Neither the arsenic concentrations in biological samples at birth nor the intelligence records of children were available in Ronpiboon district. A prospective study for exploring the chronic arsenic effects in children could not be performed in the limit time. To clarify this association, further research should be conducted in a follow-up study. However, the finding of an inverse association between arsenic concentrations in hair and the IQ of the children living in Ronpiboon district is sensitive to public concern. It demands immediate proper management from the appropriate organizations.

**Limitations of the Study Design**

The study was a cross-sectional design. It could not evaluate cause and effect because the measurements of chronic arsenic exposure and intelligence were made at the same point in time. Thus, it is impossible to determine a causal relationship. A better study design would be to undertake a prospective study of a birth cohort to relate a longitudinal assessment of arsenic exposure from birth to subsequent measures of intellectual development.

The rationale of cross-sectional design in this study was as follows: (1) There was no clear evidence of a relationship between human arsenic level and intelligence in the literature. The pioneer study should be cross-sectional to explore the possibility of this relationship. (2) No arsenic biomarkers exist which reflect arsenic exposure in children since birth. The prevalence survey of arsenic level in hair of schoolchildren and in the drinking water is a first step in establishing a database. (3) The time period of the cross-sectional study was appropriate to indicate the trend of the association of hair arsenic level and intelligence. The results are more timely for use in the planning and management of problem solving. The prospective results would not be available for many years.

However, the weak point of this study was the difficulty in evaluating a causal relationship. It could not establish the time precedence of arsenic exposure, as the level of arsenic was measured at the same time as IQ. The study suggests that the IQ deficit in children is the result of excess arsenic exposure. This association can be explained by the biological plausibility and dose–response trend. The association is more plausible as study subjects were born in 1986–1989, in a period of chronic arsenic poisoning problem in Ronpiboon subdistrict. At that time, a high proportion of drinking water was contaminated with arsenic above 0.05 ppm. This birth cohort has been continuously exposed to arsenic since birth because of their non-mobility.

Another weak point of this study was the small number of children with low hair arsenic \( (\leq 1 \text{ ppm}) \) concentrations, which therefore could not be compared to the high arsenic \( (>1 \text{ ppm}) \).
ppm) children. If there were enough subjects with low arsenic exposure, the strength of association might have been greater. Therefore, future studies should screen arsenic exposure by biomarker prior to the outcome measurement. To confirm arsenic exposure, two biological samples for arsenic analysis (i.e., hair and urine) should be collected. Consequently, the ability to separate inorganic and organic arsenic in urine, needs to be developed in Thailand. Total urinary arsenic can be misleading because seafood consumption elevates urine arsenic. It is difficult to have Ronpiboon district’s residents cease consuming seafood since this area is located in the southern part of Thailand and these residents habitually consume seafood.

The association found in this study should be non-spurious because of significant risk factor control. Thus, the reasonable and reliable findings of the study are compelling. However, several methodological difficulties were overcome in the conduct of this study. They were (1) selecting an appropriate and reliable biological marker of chronic arsenic exposure, the laboratory for hair arsenic analysis by AAS method; (2) measuring intelligence with an instrument of adequate sensitivity, WISC (the WISC was administered by experienced clinical psychologists); (3) identifying, measuring, and controlling for factors that might confound the arsenic effect. These factors were identified from literature reviews, and some of them were suggested by mentors, researchers, and experts; (4) calculating and recruiting a sample large enough to provide adequate statistical power to detect a small effect; and (5) avoiding bias in sample selection by simple random sampling from the children who met the inclusion criteria.

CONCLUSIONS

This study concludes that most children aged 6-9 years of Ronpiboon and Sao Thong subdistricts had elevated arsenic concentrations in hair (>1 ppm). The mean arsenic level in hair was 3.52 ppm (SD=3.58), and the median was 2.42 ppm. The range of hair arsenic was 0.48 to 26.94 ppm. The below average IQ level (<90), and the average level (90-109) represented 48.4%, and 45.7%, respectively, of total children. After controlling for risk factors, arsenic levels in hair were inversely associated with IQ (p=0.002). Arsenic levels could explain why the mean IQs were different in the groups of children with varying arsenic exposure.

The management of risk to children should be the following: (1) The health personnel of public health offices in Ronpiboon district and Nakorn Si Thammarat province should monitor the health status of children for early detection of abnormal IQ findings. Especially, children who have high arsenic hair concentrations need to have frequent physical examinations. (2) The curriculum at primary education level needs to be revised for the children with poor IQ by the Ministry of Education and the Ministry of Public Health. (3) The children with IQs below average should receive special teaching in school.

The important implementation is the limitation of chronic arsenic exposure from ingestion as follows: (1) The inhabitants in Ronpiboon and Sao Thong subdistricts need to discontinue using well-water for drinking and food preparation. (2) The organizations responsible should inform the community leaders, inhabitants, and students in Ronpiboon district about the severity of chronic arsenic poisoning that might retard the intelligence of children. This information is important to parents, and it is hopefully the trigger for awareness of contaminated arsenic ingestion. (3) Sufficient distribution of safe drinking water needs to be provided for residents of Ronpiboon and Sao Thong subdistricts. (4) The monitoring of drinking water in these critical areas should be established.

In order to clarify the association between arsenic and intelligence, studies should be designed and performed for confirmation in the form of a longitudinal study beginning at birth. These children should be followed up for evaluation of prolonged or permanent intellectual impairment.
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