



BLOOD LEAD LEVELS IN CHILDREN WITH SEIZURE DISORDER

Paediatrics

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ABSTRACT

Background: Raised lead levels affects neurological development of brain. Children are more prone for toxic effects of lead as compared to adults. **Aims And Objectives:** To measure blood lead levels in children with epilepsy and compare them with healthy neurologically normal children. To study the source of lead exposure in these children.

Material & Methods

Design: Case control study.

Setting: Tertiary care hospital.

Participants: Cases –Thirty four epilepsy children and 34 neurologically normal, age and sex matched controls.

Methods: Clinical and demographic details were recorded as per proforma. Detailed environmental history was recorded to know the source of exposure to lead. These children were investigated and treated as per protocol. Venous blood was collected in EDTA vial for analysis of blood lead levels. Lead levels were estimated by Shimadzu Flame AA-6800 (Atomic Absorption Spectrophotometer). Data was analysed using SPSS version 17. $P < 0.05$ was taken as significant. **Result:** Mean blood lead levels were $4.16 \pm 2.39 \mu\text{g/dL}$ in epilepsy cases and $1.88 \pm 2.18 \mu\text{g/dL}$ in these controls ($P < 0.001$). In epilepsy subjects it was found that mean blood lead levels were significantly increased ($p = 0.03$) if source of water supply is through pipeline. No correlation was found between haemoglobin and blood lead levels in cases and controls. **Conclusion:** Blood lead levels were higher in children with epilepsy. Although most of the children in the study had blood lead levels $\leq 5 \mu\text{g/dL}$.

KEYWORDS

INTRODUCTION

Environmental lead is a global issue. Several studies have shown lead levels as low as 1-3 $\mu\text{g/dl}$ are associated with subclinical toxicity (1). Children are more vulnerable to raised lead levels because of increased risk of exposure and biological susceptibility to lead as compared to adults. The neurobehavioural changes associated with early exposure to lead appears to be persistent and irreversible(1,2). In children with seizure disorder raised lead levels may further impair their cognitive abilities. Lead as aetiology of neurological diseases like lowering of seizure threshold is also being investigated in animal studies (3).

The Centers for Disease Control and Prevention (CDC) recommends reference level of 5 $\mu\text{g/dl}$ to identify children who have been exposed to lead and who require case management (4). Till date only few studies have evaluated blood lead levels in children with neurological disorders (5,6,7). These have been carried out in a small group of children, without any correlation with detailed environmental history. Hence the present study was planned to estimate blood lead levels in epilepsy cases and to compare them with healthy neurologically normal children. To know the source of exposure to lead in these children detailed environmental history was evaluated and correlated with lead levels.

SUBJECTS AND METHOD

The study was conducted at a tertiary care hospital after getting an approval from the institutional ethical committee. The study protocol was fully explained to the parents / guardian and written informed consent was obtained. A total of 68 children (34 cases and 34 controls) were enrolled in the study. Thirtyfour developmentally normal children 2-12 years of age with generalized tonic clonic epilepsy or motor partial epilepsy were enrolled. They were receiving single antiepileptic drug for at least 6 months. Diagnosis of epilepsy was made as per definition- child with two or more unprovoked seizures. Thirty four age and sex matched neurologically normal children attending outpatient department with minor ailments other than CNS disorders were enrolled as controls. Among children with epilepsy, children with developmental delay or genetic syndromes were excluded. Children with chronic liver disease or kidney disease were excluded from the study.

Data Collection

All baseline clinical characteristics and demographic data was recorded. Anthropometric parameters i.e. weight, height and head circumference were measured as per standard method. Detailed

environmental history adapted from WHO(8) was recorded to know the source of exposure to lead which included general condition of the residence and school in which child spends time, evidence of peeling paint, any recent renovations to the house, sources of smoke and dust near the house, measures attempted by the family to control dust and dirt. It also included abnormal habits in children like history of pica and washing hands before meals. Source of drinking water, type of food consumed and occupations of household members related to lead exposure was also recorded.

Investigations & Analysis

All study subjects underwent neuroimaging and other investigations as per protocol for establishing etiology. Study subjects and controls underwent measurement of haemogram, serum bilirubin and blood urea. For the purpose of analysis of lead levels, 1.5 ml of venous blood sample was drawn. Subsequently 0.5 ml of blood sample was taken in 100 ml digestion flask fitted with 30 cm long air condenser and 5.0 ml distilled HNO_3 was added to each sample. The contents were heated at 80°C for 30 min. After cooling 1.5 ml of concentrated perchloric acid (70%) was added and sample was heated again at 250°C with occasional shaking till white fumes evolved. Clear solution was cooled and transferred into a 10 ml measuring flask. The volume was made up upto 10 ml with de-ionized water. Thus, obtained sample was filtered by using syringe filter of 0.45 micron pore size (RFCL Ltd, New Delhi) and the metal level were analyzed by Shimadzu Flame AA-6800 (Atomic Absorption Spectrophotometer) from Delhi University.

Statistical Analysis

The data were entered into Microsoft Excel worksheet and analysed using SPSS Version 17.0. Mean blood lead levels were compared using unpaired Student-t test. For comparison of qualitative variables, Chi-square test was used. $P < 0.05$ was taken as significant.

RESULTS

A total of 68 children were recruited and evaluated which included 34 cases and 34 controls. Age and sex distribution was same in both groups. In epilepsy cases 16 had generalised tonic clonic seizures, 15 had complex partial seizures and rest 3 had simple partial seizures. Most of the patients were receiving either valproate 19 (55.9%) or carbamazepine 14 (41.2%). MRI was done in all cases of epilepsy. Neuroimaging was normal in 12 (35.3%) cases, rest 22 (64.7%) had abnormal MRI findings. MRI revealed neurocysticercosis in 17 (50.0%) cases.

Table I shows the comparison of blood lead levels amongst cases and

controls. The results revealed that the blood lead levels were higher in cases as compared to controls ($p < 0.001$).

Table II shows the distribution of blood lead levels amongst cases and controls. The results revealed that 14 (48.5%) cases had blood lead levels $5 \mu\text{g/dl}$, while only 2 (13.23%) controls had blood lead levels $5 \mu\text{g/dl}$ and the difference was found to be statistically significant ($p < 0.001$). No study subject had blood lead levels $10 \mu\text{g/dl}$

Table III shows the relation of environmental factors with mean blood lead levels

In epilepsy subjects it was found that mean blood lead levels were significantly increased ($p = 0.03$) if source of water supply is through pipeline.

When the blood lead levels were correlated with hemoglobin in cases and controls it was seen that there was no correlation between the blood lead levels and hemoglobin in either of the two groups ($p > 0.05$). There was no significant difference with age and sex in the mean blood lead levels ($p > 0.05$).

DISCUSSION

Blood lead levels in children with seizure disorder are important as raised lead levels causing lowering of seizure threshold been shown in mice studies (3).

In our study blood lead levels in children with epilepsy were $4.16 \pm 2.39 \mu\text{g/dl}$ compared to $1.88 \pm 2.18 \mu\text{g/dl}$ in controls ($p < 0.001$). Most of the children with epilepsy did not have lead levels $5 \mu\text{g/dl}$ requiring intervention. Raised lead levels may affect cognition in these children. Similar difference in epilepsy cases and controls was seen in study by Kumar et al (5) in which blood lead levels were $19.33 \pm 16.94 \mu\text{g/dl}$ in CP children $11.96 \pm 10.97 \mu\text{g/dl}$ in controls with ($p < 0.05$). Similarly in the study by Ahamed et al (6) lead levels were $18.60 \pm 7.93 \mu\text{g/dl}$ in children with neurological disorders and $10.37 \pm 5.08 \mu\text{g/dl}$ in controls with ($p < 0.05$). Another study by Mahmoudian et al (7) demonstrated higher lead levels in children with neurological disorders as compared to controls ($p < 0.01$).

In our study 14 (41.17%) epilepsy cases vs 2 (5.88%) controls had levels $5 \mu\text{g/dl}$ ($p < 0.001$). None of the children had blood lead levels $10 \mu\text{g/dl}$. Environmental and dietary education was given to children with lead levels $5 \mu\text{g/dl}$. Behavioural modification such as reducing pica and dietary counseling to ensure sufficient intake of essential elements like calcium and iron was also advised as per recommendation of CDC (9).

In spite of significant difference in mean levels of cases and controls, the levels in our study were lower as compared to previous studies. A fall in lead concentration has been demonstrated after phasing out of lead from petrol worldwide. Singh et al (10) conducted a study and proved that lead levels have declined in the Indian environment after the petrol lead phase out programme. The results of this study showed that mean blood lead levels of children from Mumbai, Chennai, Bangalore, Amritsar and Lucknow urban centers have fallen from $18.1 \mu\text{g/dl}$ in leaded petrol phase to $12.1 \mu\text{g/dl}$ in the unleaded petrol phase, hence the explanations for results in our study.

The correlation of environmental history with mean blood levels revealed that water supply through pipeline was associated with raised lead levels. There were 26 (76.47%) cases having water supply through pipeline, lead levels being $4.32 \pm 2.43 \mu\text{g/dl}$ compared to $2.50 \pm 0.86 \mu\text{g/dl}$ in rest ($p = 0.03$).

When the blood lead levels were correlated with hemoglobin in cases and controls, there was no correlation between the hemoglobin and blood lead levels in either of the two groups. However in the study conducted by Jain et al (11) in 2005 it has been shown that that children with higher blood lead levels have a higher incidence of anemia.

Although mean blood lead levels were higher in children with seizure disorder as compared to their age and sex matched controls, none of children with epilepsy had blood lead levels $10 \mu\text{g/dl}$. Raised lead levels in children with neurological disorders may further decline their already compromised cognitive and intellectual functioning. Whether routine estimation of lead levels will be cost effective in these children needs to be studied. Fledman et al. (12) concluded that routine lead estimation in a child psychiatric ward is not cost effective.

Further studies are required to document the clinical effects of lead levels.

Table I: Comparison of Mean Blood lead levels amongst Cases and Controls

Parameter	Cases	Controls	P-value	Mean Difference	95% CI
Mean Blood Lead Levels (Mean \pm SD)	4.16 ± 2.39	1.88 ± 2.18	< 0.001 (S) *	2.28	1.17 to 3.38

*The mean difference is significant at $P < 0.05$ using unpaired T test

Table II: Distribution of Blood Lead Levels amongst Cases and Controls

Blood lead levels ($\mu\text{g/dl}$)	Cases	Controls	P value
< 5	20(58.82%)	32(94.11%)	< 0.001 (S) *
5	14(41.17%)	2(5.88%)	
< 10	34(100.0%)	34(100.0%)	
10	0	0	

The mean difference is significant at $P < 0.05$ using Chi-square test

Table III: Relationship between environmental factors and mean blood lead levels in epilepsy subjects

		Number n(%)	Mean blood lead levels ($\mu\text{g/dl}$)	p-value
Peeling paint on woodwork, furniture and toys	Present	8(23.53%)	4.01 ± 2.10	0.845
	Absent	26(76.47%)	4.20 ± 2.51	
Recent renovations or repairs of the house	Present	9(26.47%)	5.34 ± 2.91	0.084
	Absent	25(73.53%)	3.73 ± 2.07	
Other sites which child spends time	Yes	34(100.0%)	4.16 ± 2.39	
	No	0(0%)		
Outdoor play areas contaminated soil	Present	32(94.1%)	4.27 ± 1.19	0.946
	Absent	2(5.88%)	4.15 ± 2.45	
Smoke or dust from external sources	Present	26(76.47%)	4.28 ± 2.45	0.980
	Absent	8(23.53%)	3.75 ± 2.25	
Smelters, metallurgical industries, battery recycling activity and open burning of waste	Present	8(23.53%)	3.95 ± 2.81	0.789
	Absent	26(76.47%)	4.22 ± 2.30	
Pica	Present	8(23.53%)	5.37 ± 2.31	0.101
	Absent	26(76.47%)	3.78 ± 2.32	
Hands washed before meals	Present	11(32.35%)	5.10 ± 2.55	0.204
	Absent	23(67.65%)	3.70 ± 2.22	
Occupation of household members related to lead exposure	Present	10(29.41%)	4.57 ± 2.48	0.410
	Absent	24(70.59%)	3.87 ± 2.34	
Water supply	Pipeline	26(76.47%)	4.32 ± 2.43	0.030*
	Under-ground	8(23.53%)	2.50 ± 0.86	

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