

Lead (Pb) Toxicity Trigger Schizophrenia in Battery Workers of North Region of India

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Abstract

Objectives: Total production of Pb acid batteries in India is about 8 million per year and nearly 10,000 Kg of Pb is consumed in the production of batteries. 11.35 Kg of Pb is released to the environment from production of 1000 batteries. The objectives of present study were to correlate high blood lead (Pb) levels in lead exposed battery workers with elevated risk of moderate and severe schizophrenia.

Methods: The study was conducted on 135 subjects divided into study and control groups. The inclusion criteria for study group were age between 20 to 40 years, exposure to Lead (Pb) more than five years, BMI less than 25 and having no any systemic diseases. The lead exposed subjects were taken from battery workshops of Lucknow city. Recruited subject were explained about the study protocol.

Results and Conclusion: The mean Pb level in cases were found 35.04 ± 13.39 ($\mu\text{g/dl}$) and control were 5.53 ± 1.75 ($\mu\text{g/dl}$) which are significantly ($p < 0.001$) different and exceptionally higher as compared to controls. The battery workers who were exposed ≥ 10 years have increases blood lead (Pb) level and decrease hemoglobin level in body and become mental disorder, who suggest for risk of moderate and severe schizophrenia

Keywords: Battery Workers; Lead; Brain Neurons; Schizophrenia; Neurodevelopment Disorders

Introduction

Lead (Pb)

Lead is an environmentally persistent toxicant that may cause various types of physiological and pathological disorders in human beings. Most lead used by industry comes from mine ores ("Primary") or from recycled scrap metal or batteries ("Secondary"). However, most lead today is "secondary" lead, obtained from lead-acid batteries. It is reported that 97% of these batteries are being recycled. The largest industrial use of lead today is for the production of lead batteries, extensively used in houses and automobile industries [1].

Workers of lead refining, soldering, steel welding and battery manufacturing plants experience the highest and most prolonged occupational exposure to lead (Pb) hence are vulnerable to lead toxicity. Total production of Pb acid batteries in India is about 8 million per year and nearly 10,000 Kg of Pb is consumed in the production of batteries. 11.35 Kg of Pb is released to the environment from production of 1000 batteries [2].

Prevalence of Lead (Pb) Toxicity (In 2000)

In India approximately 51% Population had blood lead levels > 10 $\mu\text{g/dl}$, and 13% Population had values > 20 $\mu\text{g/dl}$. The proportion of children with levels > 10 $\mu\text{g/dl}$ ranged from 40% in Bangalore and 62% in Mumbai [3]. Thus chronic exposure to environmental lead remains a significant public health issue among low-income populations of Uttar Pradesh as well as India, because many workers like battery repairers are prone to lead exposure and Neurobehavioral disorder like- schizophrenia.

Schizophrenia

According to World Health Organization (WHO survey report-2014) 26 million people are suffering from Schizophrenia in the World. In India 40 to 45 lakhs people are suffering from Schizophrenia. According to clinical diagnosis the attended are also suf

fering from Schizophrenia who lives a long time with severe patients. It is assumed that there is suffering one patient of Schizophrenia in 1000 of peoples, but the clinician would not identified this disease. In spite that People are leave the patients in the society as prove as mad.

Thus it is the major problem in the society as well as in India for those people who are living in environment or battery workers who are direct contact with Lead (Pb) exposure from Lead (Pb) acid battery manufacturing Industries.

Schizophrenia is a mental disorder characterized by a breakdown in thinking and poor emotional responses. Schizophrenia causes significant social and work problems. Symptoms begin typically in young adulthood and about 0.3-0.7% of people are affected during their lifetime [4]. Schizophrenia does not imply a “split personality”, or “multiple personality disorder”—a condition with which it is often confused in public perception [5]. Rather, the term means a “splitting of mental functions”, reflecting the presentation of the illness [6]. The disorder is thought to mainly affect the ability to think, but it also usually contributes to chronic problems with behavior and emotion. People with schizophrenia are likely to have additional conditions, including major depression and anxiety disorders; the lifetime occurrence of substance use disorder is almost 50% [7]. Social problems, such as long-term unemployment, poverty, and homelessness are common. The average life expectancy of people with the disorder is 12 to 15 years less than those without. This is the result of increased physical health problems and a higher suicide rate (about 5%) [8].

Relationships between early exposure to lead and neuropsychological abnormalities have been observed throughout the life course. In a prospective study conducted in Cincinnati, prenatal and average childhood blood lead concentrations were reported to be associated with increased delinquent behavior later in life [9]. This suggests that prenatal lead exposure may be a risk factor for other adolescent and adult-onset outcomes, possibly psychiatric disorders. Schizophrenia is one plausible candidate, as some of its premorbid features such as reduced attention, neurocognitive impairment, and diminished educational attainment strongly resemble the behavioral deficits associated with lead exposure [10].

Prevalence of schizophrenia (In 2000)

In 2000, the World Health Organization found the prevalence and incidence of schizophrenia to be roughly similar around the world, with age-standardized prevalence per 100,000 ranging from 343 in Africa to 544 in Japan and Oceania for men and from 378 in Africa to 527 in Southeastern Europe for women [11].

Prevalence of schizophrenia (In 2011)

Schizophrenia affects around 0.3-0.7% of people at some point in their life, or 24 million people worldwide as of 2011 [12]. It occurs 1.4 times more frequently in males than females and typically appears earlier in men the peak ages of onset are 25 years for males and 27 years for females [13]. It causes approximately 1% of worldwide disability adjusted life years and resulted in 20,000 deaths in 2010 [14].

Methods

The current study was designed to assess the relationship between lead exposed battery workers and schizophrenia. This study was case - control study in which schizophrenia and related disorders had been diagnosed. The study was conducted on 135 subjects divided into study and control groups. The inclusion criteria for study group were age between 20 to 40 years, exposure to Lead (Pb) more than five years, BMI less than 25kg/m² (non obese) and having no any systemic diseases. The inclusion criteria for control group were age between 20 to 40 years, not known exposure, BMI less than 25kg/m² (non obese) and having no any systemic diseases. The lead exposed subjects were taken from battery workshops of Lucknow city. Recruited subject were explained about the study protocol. The Structured Clinical Interview for diagnostic of mental disorders was used to verify diagnoses of schizophrenia.

Blood Lead Estimation

Venous blood samples were taken in a climate-controlled room before the beginning of a regular workday (between 7:00 AM and 9:00 AM), after the subjects had fasted for 10hrs. The subjects were seated while samples were drawn. Blood specimens for lead measurement were drawn into a 10-ml polypropylene tube with sodium heparin as anti-coagulant and stored at -20 °C until assayed. The Blood Lead Level (BLL) was estimated in µg/dl by Lead Care- II system, based on atomic absorption furnace in both the groups.

Diagnosis of schizophrenia through Questionnaires methods

According to standardized procedures to assess mood, symptoms, and functioning in the weeks prior to the day of testing. Questionnaires methods were used to assess schizophrenia. The assessments included measures of psychotic symptoms (PANSS), anxiety (Beck Anxiety Inventory, BAI), depression (Beck Depression Inventory, BDI-II), and self-reported functioning Independent Living Skills Survey, ILSS), Mood and stress (Sad mood, Happy mood, Stress severity, Anxious mood) and then assess the functional behavior and environment, Psychotic Symptoms, etc.

Diagnosis of schizophrenia through MRI

Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The subjects were advised for MRI of brain who was exposure from more than 10 years and the blood lead (Pb) levels was more than 40 µg/dl.

Statistical analysis

Data has been presented as the mean \pm SD of all the observations. The values from the two groups (exposed and control subjects) were compared by independent Student's 't' test. Non-parametric alternative Mann-Whitney U test was also applied where the data was not normal or heterogeneous. Odds ratio with 95% CI was used as a measure of effect size using binary logistic regression analysis. A two-sided ($\alpha=2$) $p<0.05$ was considered to be statistically significant. All the analyses were performed on STATISTICA (version 6.0) software. Data were calculated by M.P. Negi, Statistician in Central Drugs Research Institute (CDRI), Lucknow.

Results

Basic characteristics

The present study evaluates the relationship between lead exposed battery workers and schizophrenia. Total 65 men battery workers (cases) were recruited. The age matched 70 healthy men were also recruited served as controls. The basic characteristics of two groups are summarized in Table 1. The mean age, height, chest circumference and hip circumference were slightly higher in cases than controls while weight, BMI and abdominal circumference were higher in controls than cases. However, all basic characteristics did not differed ($p>0.05$) between the two groups i.e. found to be statistically the same.

Characteristics	Controls (n=70)	Cases (n=65)	P -Value
Age (yrs)	38.16 \pm 6.82	38.34 \pm 7.98	0.887
Height (cm)	163.56 \pm 5.20	163.94 \pm 6.31	0.701
Weight (kg)	65.26 \pm 6.18	63.15 \pm 8.09	0.091
BMI (kg/m ²)	24.82 \pm 2.34	24.41 \pm 2.26	0.306
Chest circumference (cm)	82.51 \pm 3.26	82.83 \pm 3.80	0.604
Abdominal circumference (cm)	72.47 \pm 3.69	68.94 \pm 5.93	0.205
Hip circumference (cm)	80.74 \pm 4.57	82.25 \pm 7.38	0.154

Table 1: Basic characteristics (Mean \pm SD) of two groups

Biochemical parameter

The biochemical parameter (Pb and Hb%) levels of two groups at presentation are summarized in Table 2. The mean Pb level in cases was found significantly ($p<0.001$) different and exceptionally higher as compared to controls. In contrast, the mean hemoglobin (Hb%) level in cases was found significantly ($p<0.001$) different and lower as compared to controls. In cases, the increase in Pb and decrease in Hb% showed 2.47 (OR=2.47, 95% CI=1.54-4.71) and 1.32 (OR=1.32, 95% CI=1.11-3.47) fold more variations respectively as compared to controls.

Parameters	Controls (n=70)	Cases (n=65)	P -Value	OR (95%CI)
Pb (µg/dl)	5.53 \pm 1.75	35.04 \pm 13.39	<0.001	2.47 (1.54-4.71)
Hb (%)	12.06 \pm 1.55	9.47 \pm 1.72	<0.001	1.32 (1.11-2.47)

Table 2: Biochemical parameter levels (Mean \pm SD) of two groups

Radiological parameter

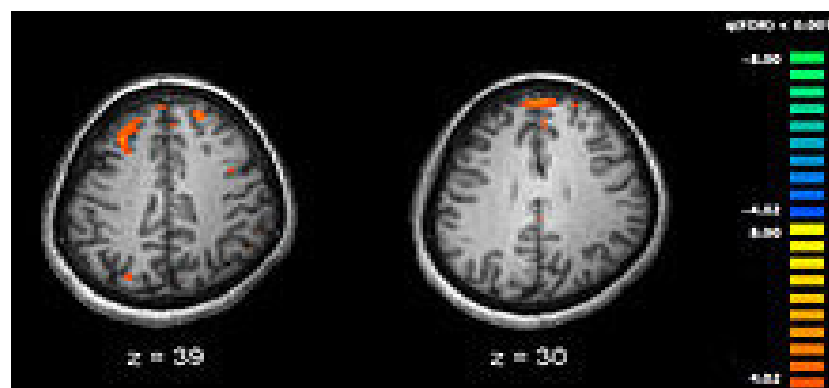


Figure 1: Neurological disorder due to Lead (Pb) Toxicity and schizophrenia

The functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people who are highly direct exposed lead (Pb) toxicity in battery Industries and Shops were diagnosed with schizophrenia. There are two image of brain with areas that were more active in healthy person (controls groups) than in battery workers (cases) suffering from schizophrenia shown in orange coloured, during an fMRI study of working memory (Figure 1).

Schizophrenia is associated with subtle differences in brain structures, found in 40 to 50% of cases, and in brain chemistry during acute psychotic states. Studies using neuropsychological tests and brain imaging technologies such as fMRI and PET to examine functional differences in brain activity have shown that differences seem to most commonly occur in the frontal lobes, hippocampus and temporal lobes. Reductions in brain volume, smaller than those found in Alzheimer’s disease, have been reported in areas of the frontal cortex and temporal lobes. It is uncertain whether these volumetric changes are progressive or preexist prior to the onset of the disease. These differences have been linked to the neurocognitive deficits often associated with schizophrenia. Because neural circuits are altered, it has alternatively been suggested that schizophrenia should be thought of as a collection of neurodevelopmental disorders.

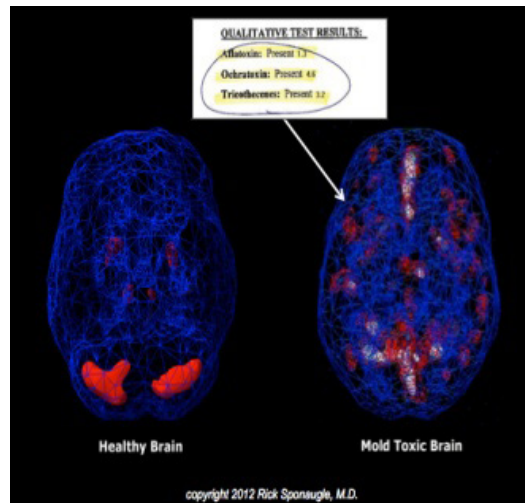


Figure 2: Neurological (Panic) Disorder and Bipolar Symptoms Lead (Pb) Toxicity

The extra red and white areas seen on the Lead (Pb) toxic brain scan represent severely over active regions that were causing panic disorder and bipolar symptoms in Daniel, a 39 year-old battery workers who developed Lead (Pb) toxicity within 17 years of living in battery Industries (Figure 2).

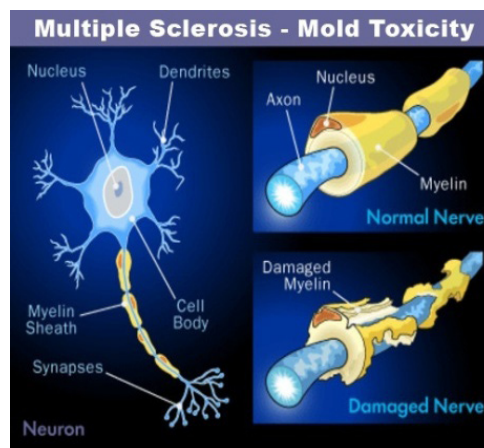


Figure 3: Multiple Sclerosis due to Lead (Pb) Toxicity

Lead (Pb) toxins destroy the myelin sheath on brain neurons causing the classic “white spots” seen in Multiple Sclerosis. When we diagnoses over 65 battery workers (cases) within three years with Multiple Sclerosis via MRI of the brain, than we find out Many of these battery workers who were direct severe exposure of lead (Pb) toxicity more than 10 years in Industries are become Multiple Sclerosis (Figure 3).

Discussion

Our study represents Lead (Pb) exposure as a risk factor for an adult psychiatric disease. Lead was widely distributed throughout urban areas as well as rural areas, battery Industries, shops of different part of Lucknow city. Although BPb levels in the United States have declined, lead exposure continues to be of great concern.

A variety of findings suggest that interactions between ALA-D polymorphisms and lead exposure may affect long-term outcomes, including differences in neuropsychological effects of lead exposure [15]. It is possible that a specific ALA-D polymorphism may be a risk factor for schizophrenia, either independently or through interactions with blood lead. In considering lead exposure during development as a risk factor for adult mental illness, both direct and indirect mechanisms may be postulated. Direct mechanisms could involve physical interactions between lead (Pb) and the developing nervous system, interfering with growth, differentiation, or structural development. Both have been implicated in the pathogenesis of schizophrenia [16]. Thus, it is possible that Lead (Pb) toxicity from lead acid battery Industries and shops were elevate the risk of schizophrenia spectrum disorders, independently.

Mold toxic patients experience a gradual progression as they slowly accumulate more mold toxins, their symptoms usually begin with insomnia, then as they spend more time in living and working in mold toxic buildings, their symptoms progress from insomnia, to insomnia and day time anxiety. As they accumulate more toxins, their anxiety can progress into full blown panic disorder and ultimately, in the most severe cases of mold toxicity, patients can develop bipolar symptoms of rage and paranoia. It is the increased activation of Glutamate and PEA nerve receptors throughout the body that produces an over electrified nervous system, thus producing symptoms of anxiety, insomnia, panic disorder, bipolar syndrome and fibromyalgia [17].

Therefore on the basis of our study battery workers who are directly expose or inhaled lead (Pb) toxicity from battery through skin, nose, mouth, and gastrointestinal, which are accumulated and circulated through whole blood to the nervous system of brain and damage gradually neuron. After few days it develops mental disorder characterized by a breakdown in thinking and poor emotional responses. The delusions, such as paranoia; hearing voices or noises that are not there; disorganized thinking; a lack of emotion and a lack of motivation and subject were suffer from irritation, perception, depression and anxiety disorders. Therefore the battery workers who are gradually become psychotic disorder i.e. schizophrenia.

Conclusion

The mean Pb level in cases were found 35.04 ± 13.39 ($\mu\text{g}/\text{dl}$) and control were 5.53 ± 1.75 ($\mu\text{g}/\text{dl}$) which are significantly ($p < 0.001$) different and exceptionally higher as compared to controls. In contrast, the mean hemoglobin (Hb%) level in cases were found 9.47 ± 1.72 Hb% and control were 12.06 ± 1.55 Hb% which are significantly ($p < 0.001$) different and lower as compared to controls.

In summary, in this study, relatively high blood lead (Pb) levels in lead exposed battery workers with lead exposure more than ten years were significantly associated with elevated risk of moderate and severe schizophrenia. We found those battery workers who were exposed ≥ 10 years have decrease hemoglobin level in body and they all are become mental disorder, irritation, perception, confusion, breakdown in thinking and poor emotional responses who suggest for risk of moderate and severe schizophrenia.

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