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Association between Blood Lead (BLL) Level Concentration and Tremor in Highly Exposed Battery Workers at Manufacturing Industries of Lucknow City

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Abstract:

Objective: Tremor is one of the most commonly encountered neurological problems, and it may be a feature of a variety of neurological diseases. Despite tremor among very common in elderly, there are very limited data on the role of environmental exposures that are potentially modifiable. Lead is an environmentally persistent toxicant that may cause various types of physiological and pathological disorders in human beings.

Material and Method: 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 & industries of Lucknow city. Recruited subject were explained about the study protocol.

Result: The mean Pb level in cases were found 35.04 ± 13.39 (µg/dl) and control were 5.53 ± 1.75 (µg/dl) which are significantly ($p < 0.001$) different and exceptionally higher as compared to controls. Higher value of lead (Pb) level disturbed the balancing power and motor nerve of brain therefore tremor are developed in arm and leg. .

Conclusion: The battery workers who were exposed ≥10 years have increased blood lead (Pb) level and decrease hemoglobin level in body and suffering from tremor disorder, who suggest for risk of moderate and severe neurological manifestation like tremor.

Keywords: Battery workers; Lead (Pb); Cerebellar part & Basal ganglia; Termers

Introduction

Tremor is one of the most commonly encountered neurological signs, and it may be a feature of a variety of neurological diseases. Tremor is elderly in common; there are limited data on the role of environmental exposures that are potentially modifiable. Lead is an environmental neurotoxicity that has been suspected as a risk factor for (ET) essential tremors[1]. Case–control studies in two settings have examined the association between elevated blood lead concentration and ET[2-5]. According to the Hu et al. (1998)[6] and Rabinowitz (1991)[7] when the concentration of blood lead is to be higher than it may be assumed that the risk of ET may be also higher. However, blood lead has a half life of approximately 30 days. If lead induced neurotoxicity results in ET, or more broadly in action tremor, it is likely chronic exposure may be more relevant. To examine the association between chronic lead exposure and action of tremor, we used data from participants in the Department of medicine, King George's Medical University U.P., Lucknow.

The main toxic effects of lead are on the brain and nervous system. In adults, high levels of lead can cause headaches and problems with mood, thinking, and memory. It may also damage peripheral nerves, which can cause tremors or weakness in fingers, wrists, or ankles. Adults whose work exposes them to lead have been shown to develop nervous system problems even at relatively low blood lead levels. Lead poisoning in children can lead to lower intelligence, stunted growth, impaired hearing, and behavioral and learning problems. These

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problems can even appear in children whose mothers were exposed to lead while pregnant with them.

According to survey of WHO 8 million Lead (Pb) is produced per year in India, and about 10,000 Kg of lead is consumed in the production of battery and it is assumed that 1,000 batteries released nearly 12 Kg of lead in and around the environment. So therefore it observes from environment through the skin, respiration, by nose and mouth, by food material, gastrointestinal etc. When it observed in the body, get accumulated and goes a physiological & biochemical reaction with enzyme and gradually it change the physiological and neurological activity. It is assumed that when it get accumulated in the brain it disturb the balancing of body and causes termer of hand and neck. The battery workers have more sign and symptoms in cerebellar part and abnormalities referable to basal ganglia (e.g. rest tremors, subclinical termers, sign of bradykinesia, and cognitive deficit) [8] . These diseases are highly prevalent in general population[9] and observed in all population. The pathogenesis of this progressive and often disability disease is poorly understood[10] although there is evidence of cerebellar involvement[11].

On the basis of above study we hypothesized that the battery worker who are directly exposed the lead (Pb) in battery Industries are good chance of accumulation of lead and developed neurological disorder mainly tremor.

Methods

The current study was designed to assess the association between highly lead (Pb) exposed battery workers and Tremor. This study was case - control study in which Tremor 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 25 and having no any systemic diseases. The lead exposed subjects were requited from battery workshops/ industries of Lucknow city. Each recruited subjects were explained about the study protocol. The Structured Clinical Interview for diagnostic of neurological disorders was used to verify diagnoses of Tremor.

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 Termers

Toxic neuropathies are often misdiagnosed as there are no easily available specific or biological tests for the diagnosis. Toxic neuropathies are suspected on the basis of clinical examination and electro diagnostic features.

Clinical examination, interview and questionnaires

An occupational medicine physician (T.N) conducted the clinical examinations and performed the interviews on all participating workers. The physical examination concerned principally the hands and upper limbs with a focus on neurological and musculoskeletal disorders. A standard procedure was followed, including a basic neurological examination of the hands. In the medical interview, the participants were asked to give a detailed history of previous and current diseases and symptoms, medication, alcohol consumption, and nicotine use. Nicotine use concerned either smoking or snuff use. A supplementary questionnaire was also administered covering the above-mentioned information. The different examinations and tests were all conducted in 1 day starting with the medical examination, followed by (in given order) testing of manual dexterity; finger and hand strength; touch, vibrotactile, and thermotactile sense; and the quantitative tremor measurements.

Vibration exposure assessment

With the help of questionnaire and measurements all the information on hand-arm vibration (HAV) exposure was collected. The battery workers noted about time of exposure, age of subject, working time in year, lead (Pb) exposure in minutes per day, and type of battery refilling mostly lead acid battery and work task. Measurements were done by standardized scheme during representative work. The main tools used by the participating battery workers were grinders, die grinders and hammers with vibration intensity ranging from 1.5 to 10 m/s^2. HAV exposure was given in time (hours) and acceleration level (m/s^2) in accordance with International Organization for Standardization (ISO) guidelines (European Council; ISO: 5349-1; ISO: 5349-2). The product of exposure hours (h) and of hand-arm acceleration (m/s^2) was used as the cumulative HAV exposure dose (unit h m/s^2). The battery workers who operates a hand-held vibrating tool with the intensity of 2.5 m/s^2 (the EU action level) during 6 h per working day and 200 working days per year for 1 year ends up with an exposure dose of 4,000 h m/s^2. Current exposure, as in using hand-held vibrating tools at the time of follow-up (2008), was recorded in acceleration (m/s^2) and given in A(8) values (ISO:5349-1) that ranged from 0.0 to 2.1 m/s^2 with a mean of 0.50 m/s^2 and standard deviation (SD) of 0.80 m/s^2.

Quantitative tremor measurements

We informed the entire subjects in advance to avoid doing from HAV exposure and nicotine use, on the day of testing. The tremor measurements were done by an experienced researcher. The CATSYS Tremor Pen® was used for measuring postural tremor (DPD 2000). The equipment consists of a biaxial micro-accelerometer embedded in a low-mass stylus (12 cm × 0.8 cm), which is sensitive when perpendicular to the central axis of the stylus, and has been standardized and validated (Despres et al. 2000; Edwards and Beuter 1997). For the testing procedure, the subjects were advised for sit in a chair and rest after than hold the stylus as they would hold a writing pen, with the elbow joint bent at an angle of 90°, and to avoid contact. The stylus was held horizontally about 10 cm in front of the navel. Tremor was recorded successively in each hand over 16.4 s. The subjects were asked to look at the tip of the stylus and breathe normally during recording. The tremor registrations were dis-

played in real time on a time axis plot on the computer screen. Fourier transformation was used to determine the power distribution across a frequency band varying from 0.9 to 15 Hz. The tremor intensity, center frequency, frequency dispersion and harmonic index were calculated by the CATSYS software. Table 1

Table 1:
(1). Definitions of measures used to characterize postural arm tremor recorded with the CATSYS system (Despres et al. 2000; Wastensson et al. 2006)
(2). Definitions of characteristics from Danish Product, Development Ltd. (DPD 2000)

Tremor intensity (m/s^2)
The tremor amplitude given in root-mean-square of acceleration (m/s^2) recorded in the 0.9- to 15-Hz band. Higher values indicate more tremor
Center frequency (CF), (Hz)
The median frequency of the acceleration in the 0.9- to 15-Hz band. abnormal scores are expected to be lower
Frequency dispersion (FD), (Hz)
The standard deviation of CF indicating the degree of tremor irregularity. Regular tremor has low values of FD. Abnormal scores are expected to be lower
Harmonic index (HI)
Comparison of the tremor frequency pattern with a single harmonic oscillation. The HI decreases when the tremor is composed of many oscillations. Abnormal scores are expected to be higher

Results

Basic characteristics

The present study evaluates the association between lead exposed battery workers and Tremor. 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 2. 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. Table 2.

Table 2: Basic characteristics (Mean ± SD) of two groups.

Characteristics	Controls (n=70)	Cases (n=65)	P - Value
Age (yrs)	38.08 ± 5.62	38.13 ± 6.87	0.762
Height (cm)	163.37 ± 5.43	163.82 ± 5.73	0.624
Weight (kg)	65.35 ± 6.23	63.03± 7.26	0.078
BMI (kg/m^2)	24.64 ± 3.57	24.29 ± 2.41	0.210
Chest circumference (cm)	82.38 ± 3.12	82.72 ± 3.39	0.527
Abdominal circumference (cm)	71.32 ± 3.14	67.63 ± 5.62	0.198
Hip circumference (cm)	80.53 ± 4.36	82.18 ± 6.52	0.167

Biochemical parameter

The biochemical parameter (Pb and Hb%) levels of two groups at presentation are summarized in Table-3. 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. Table 3

Table 3: Biochemical parameter levels (Mean ± SD) of two groups.

Parameters	Controls (n = 70)	Cases (n = 65)	P - Value
Pb (µg/dl)	5.42 ± 1.61	35.13 ± 12.63	< 0.001
Hb (%)	12.36 ± 1.68	9.10 ± 1.32	< 0.001

Tremor measurements

If using two separate models for cumulative and current HAV exposure, the results were the same. The higher values of lead (Pb) resulted in a statistically significant predictor for tremor intensity in left hand, in other words higher values of lead (Pb) was responsible for frequency dispersion, resulted in a statistically significant predictor for tremor intensity in left hand, in other words higher values of lead (Pb) causes frequency dispersion in both hands, and harmonic index in both hands, it means higher values of tremor. The increasing value of lead (Pb) was also presented as statistically significant for tremor with both hands concerning tremor intensity (i.e., higher values), and concerning frequency dispersion (i.e., lower values). For the left hand, there were more lead (Pb) values for harmonic index (i.e., higher values). Center frequency showed an association for less tremor values for the right hand (i.e., higher values). Table 4 presents adjusted *R2* values, regression coefficients, *p* values of *F* tests and statistically significant predictors. In general, the adjusted *R2* values were very low and the model with center frequency for the left hand did not hold (the *p* value for *F* test was above the 0.05 level). Table 4

Table 4: Data on tremor measurement values using the CATSYS system.

Parameters	Controls (n= 70)	Cases (n = 65)	P - Value
Tremor intensity (m/s^2), R	0.118 ± 0.046	0.129 ± 0.030	< 0.001
Tremor intensity (m/s^2), L	0.110 ± 0.034	0.113 ± 0.038	< 0.001
Center frequency (Hz), R	7.12 ± 1.06	7.26 ± 0.912	< 0.001
Center frequency (Hz), L	7.01 ± 1.28	7.29 ± 1.080	< 0.001
Frequency dispersion (Hz), R	2.79 ± 0.671	2.60 ± 0.647	< 0.001
Frequency dispersion (Hz), L	3.01 ± 0.748	3.10 ± 0.685	< 0.001
Harmonic index, R	0.905 ± 0.023	0.910 ± 0.019	< 0.001
Harmonic index, L	0.886 ± 0.030	0.880 ± 0.409	< 0.001

SD standard deviation, R right hand, L left hand

Statistical analysis

Data has been presented as the mean ± 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. 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.

Discussion

The previous reports on tremor occurrence mentioned in the introduction[12,13] may possibly be explained by different interpretations of the definition of tremor. There are no clear definitions of tremor in the studies reporting tremor in HAV-exposed workers. Futatsuka et al. seem to have used interviews and Bylund et al. used a questionnaire based on "earlier surveys" from, for instance, Atroshi et al[14]. Shivers, jerks and possibly impaired manual dexterity may be mistaken for or perceived as tremor. According to loss of sensory function and/or muscular dysfunction in the hands and fingers may be associated with impaired manual dexterity, which could possibly explain symptoms that subjects describe as similar to tremor[15]. Tremor has been hypothesized to depend on acute effects of HAV exposure; however, one study with an experimental approach testing acute effects after a limited dose of HAVs showed the opposite, in other words, less tremor after exposure[16]. Lead neuropathy like motor neuropathy is rarely found in battery workers. Mean blood lead level (BLL) among the battery workers was found to be high therefore this was developed common illnesses headache, numbness of the limbs, colic pain, nausea, tremor, and lead line on the gum. High BLL was also found to be related to hypertension and anemia of the workers. The mean Pb level in cases were found 35.13 ± 12.63 (µg/dl) and control were 5.42 ± 1.61(µg/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 9.10 ± 1.32 Hb % and control were 12.36 ± 1.68 Hb % which are significantly ($p < 0.001$) different and lower as compared to controls. It is hypothesized that when the lead (Pb) is accumulated in the body, it get effected to the brain mainly motor nerves and sensory nerve by which the balancing tendency get effected and the vibration in the leg and arm becomes very highly it means develop tremors in both arm or feet of body. All tremor measurements concern postural tremor, and it cannot be entirely ruled out that effects from HAV exposure could have an impact on some other form of tremor such as, for instance, kinetic tremor or task specific tremor.

Conclusion

In this study, relatively high blood lead (Pb) levels in lead exposed battery workers were significantly associated with elevated risk of moderate and severe termers. We found those battery workers who were exposed ≥10 years and have increase value of lead (Pb) with decrease hemoglobin level, it means there were developed the neurological disorder like tremors in body and they all have symptoms of mental disorder, like irritation, perception, confusion, breakdown in thinking and poor emotional responses who suggest for risk of moderate and severe neurological disorder and disturb the physiological activity in the body, causes tremors.

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