ORIGINAL ARTICLE

Assessment of peripheral neuropathy in male hospitalized patients with lead toxicity in Iran

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Background: This study assessed the effect of lead exposure on the peripheral nervous system in 40 hospitalized patients with lead toxicity [blood lead level (BLL) >70 µg/dl] and compared their electrodiagnostic indices with the results of the control group. **Materials and Methods:** We assessed signs and symptoms of neuropathy in patients and conducted nerve conduction velocity (NCV) in patients and control groups, then compared the results between the two groups. **Results:** Average duration of exposure to lead was 10.85 years. The mean BLL of patients was 100.32 µg/dl (SD = 18.42). The most common symptoms in patients were mood and sleep disturbance (64.1%) and paresthesia (47.5%). Among the patients, all of the NCV indices in median, ulnar, and radial nerves were normal. On comparing the average indices of NCV in lead-exposed men with controls, significant reductions were noted in most of the indices and with prolonged distal motor latency and peak latency. Significant but weak correlations were found between BLL and some of the indices (P value < 0.05, r = 0.33-0.52). **Conclusion:** Comparing electrophysiological study indicators between case vs controls and considering the symptoms of patients, our study showed that patient may progress to sensory neuropathy.

Key words: Blood lead level, electrophysiological study, Iran, lead toxicity, nerve conduction velocity

INTRODUCTION

In occupational settings, chronic lead intoxication is a slow and insidious disease with variable manifestations. Fatigue, apathy, irritability, and vague gastrointestinal symptoms are early signs of chronic lead intoxication.[1] Long-term exposure can result in lead neuropathy. The classic form of lead neuropathy consists of weakness primarily involving the wrist and finger extensors.[1,2] Mild to moderate sensory dysfunction may also be evident in lead neuropathy, often with asymmetric features.[2] The most frequently observed symptom in exposed workers is sensory symptoms such as paresthesia and a pinprick sensation on physical examination.[3] Whether this neuropathy can result from lead intoxication is controversial.

The most persuasive evidence in support of the sensory neuropathy is in Latvian patients.[4] Abnormalities of nerve conduction are common among exposed individuals, but these abnormalities are mild. It is not clear whether these abnormalities predict clinical neuropathy.[4,5] Some studies have shown no correlation between blood lead concentration and the severity of electrophysiological abnormalities.[3,4] A meta-analysis by Araki *et al*. (2000) recommended further cross-sectional studies to clarify dose–response relationships of lead and effects on nerve conduction velocity (NCV),[6] while a recent meta-analysis could not show a conclusive relationship[7] In this study, we evaluated signs and symptoms of neuropathy and performed NCV tests in patients with high level lead toxicity (blood lead level (BLL) >70 µg/dl) and compare the electrophysiological values with a control group. Also, we assessed the correlation between BLL and electrophysiological values.

MATERIALS AND METHODS

Our study was conducted on 40 patients with lead toxicity (BLL > 70 µg/dl) who were admitted to Baharlu Hospital Affiliated to Tehran University of Medical Sciences during 2009. None of the patients had any history of neuropathy generating disorders (i.e., diabetes mellitus, hypothyroidism, traumatic injuries, nutritional disorders, chronic renal and hepatic disorders, malignancies, vasculitis). Our control group consisted of 62 male individuals without neuropathy and related clinical finding who were visited in the outpatient clinic for other reasons. Also, they had no history of lead exposure. The patients and controls were not specifically age-matched but they were in the same age range.

All cases were referred from a battery manufacturing company in which lead exposure was noticeable. We assessed symptoms and signs of lead toxicity in all of the patients.

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Physical examination consisted of sensory and motor examinations, deep tendon reflex (DTR), and limb power measurement. DTR was graded as normal, decreased, or absent. Also involvement of other organ systems was noted such as mood or sleep disturbances, gastrointestinal disturbances, and changes in blood pressure.

We measured general biochemical parameters including complete blood count (CBC), hemoglobin (Hgb), blood urea nitrogen (BUN), creatinine (Cr), liver function tests (LFT), and fasting blood sugar (FBS) of our patients.

NCV was done bilaterally for both groups by only one neurologist. Measurements were made with a Medelec electrophysiological system (Model MS 6). In this way following indices were measured: Sensory nerve conduction velocity (SNCV), motor conduction velocity (MCV), sensory nerve action potential (SNAP), compound muscle action potential (CMAP), distal motor latency (DML), and peak latency (PL).

Venous whole blood was sampled by a trained phlebotomist, collected in lead-free heparinized vacutainer and stored at 4°C for 2 weeks for analysis. We used a flameless atomic absorption spectrophotometer for blood lead measurement.

RESULTS

Patient and control group characteristics

All patients and controls were males with a mean (SD) age of 36.2, SD = 7.13 and 34.5, SD = 6.79 years), respectively. BLL had a range of 70-143 μg/dl with a mean of 100.32 μg/dl in patients and was in the normal range in controls (mean BLL = 9.33, SD = 18.42). The mean duration of occupational exposure was 10.85 years, SD = 4.77 (range from 1 to 21 years) in cases with a mode of 12 years of exposure.

All of biochemical parameters including CBC, BUN, Cr, LFT, FBS were in normal range values. A total of 17 cases (42.5%) had low level Hgb (below 14 g/dl).

Clinical features of lead toxicity

Among patients the most three common symptoms were mood and sleep disturbance, paresthesia, and myalgia respectively. Also impaired sensory exam and decrease of limb force were seen in 15% of cases as the most prevalent sign [Table 1]. No autonomic symptoms were noted among them. All patients (mean SBP: 114.99 ± 10.72 and DBP: 64.66 ± 6.72) and control group (mean SBP: 115.72 ± 13.25 and DBP: 67.81 ± 5.99) had normal blood pressure.

Nerve conduction studies

Considering right and left upper extremities, there were no significant differences in nerve conduction indices between two sides among all participants. Only one patient had bilateral mild axonal radial nerve neuropathy with BLL = 139, in whom the duration of exposure was 11 years. Other results are presented in [Tables 2-4].

Motor and sensory conduction velocity, amplitude of the evoked action potential and distal motor, and sensory latency in the median, ulnar, and radial nerves were normal in our patients. When the average of NCV indices in lead exposed men was compared with the average of the same indices in age-matched controls, it was noted that MCV, SNCV, SNAP, and CMA*P* values were significantly reduced and DML and PL values were significantly prolonged in patients.

Table 1: Patients' characteristics and clinical features

Symptoms	Number affected (%)
Paresthesia	19 (47.5)
Myalgia	15 (37.5)
Weakness	4 (10)
GI symptoms: Abdominal pain, constipation, nausea, loss of appetite	14 (35)
Mood and sleep disturbance	25 (64.1)
Signs	
Impaired sensory exam	6 (15)
Impaired motor exam	3 (7.5)
Decrease of deep tendon reflex	4 (10)
Decrease of limb force	6 (15)
High blood pressure	1 (2.5)

DTR=Deep tendon reflex

Table 2: Right median nerve conduction study (mean (SD))

Investigated indices in nerves	Patient	Control group	*P* value
DML	3.08 (0.25)	2.81 (0.51)	0.038
MCV	42.80 (1.5)	43.35 (0.99)	0.000
CMAP	5.32 (0.82)	5.84 0.55)	0.000
SNAP	26.4 (4.33)	27.70 (1.31)	0.028
PL	2.98 (0.32)	2.77 (0.49)	0.021
SNCV	42.83 (0.94)	43.45 (1.5)	0.000

DML=Distal motor latency (ms); MCV=Motor conduction velocity (m/s); CMAP=Compound muscle action potential (mV); SNAP=Sensory nerve action potential (μV); PL=Peak latency; SNCV=Sensory nerve conduction velocity

Table 3: Right ulnar nerve conduction study (mean (SD))

Investigated indices in nerves	Patient	Control group	*P* value
DML	2.54 (0.31)	2.33 (0.12)	0.000
MCV	42.87 (1.77)	43.35 (0.83)	0.000
CMAP	5.21 (1.09)	5.97 (0.66)	0.000
SNAP	26.05 (4.06)	26.14 (2.08)	0.877
PL	2.56 (0.27)	2.31 (0.07)	0.000
SNCV	43.20 (1.39)	44.27 (1.62)	0.81

DML=Distal motor latency (ms); MCV=Motor conduction velocity (m/s); CMAP=Compound muscle action potential (mV); SNAP=Sensory nerve action potential (μV); PL=Peak latency; SNCV=Sensory nerve conduction velocity

Pearson correlation analysis showed that there were statistically significant but weak correlations between BLL and DML in right ulna, MCV in left median, MCV in right and left ulna, SNCV in left ulna, and SNCV in left radial (P value < 0.05, r = 0.33-0.52) [Table 5].

DISCUSSION

In this study, we found that the most common symptoms in our patients (with mean of BLL: 100 µg/dl and mean exposure duration of 10.85 year) were mood and sleep disturbances (64.1%), and paresthesia (47.5%). Among patients, all of the NCV indices in median, ulnar, and radial nerves were normal. On comparing the average indices of NCV in lead-exposed men with controls, significant reductions were noted in most of the values and with prolonged DML and PL.

Comparing electrophysiological study indicators between case vs controls and considering the signs and symptoms of patients, we suggest the patients may progress to sensory neuropathy.

Some studies have reported that long-term exposure (>10 years) to lower BLL may cause mild sensory and autonomic features instead of the motor neuropathy classically attributed to lead toxicity.[5,8-17] Although our findings are consistent with these results, our patients had higher BLL. Meanwhile, according to an invited review by Thomson *et al*.,[4] occupational exposure to high level of lead for less than 5 years (BLL > 100 µg/dl) causes the classic motor form of neuropathy in patients.[4]

Since we didn't have any environmental monitoring reports, reporting on change of work processes, and measurement of BLL in previous years, we could not certainly conclude that patients had not any recent acute intoxication. However, our clinical findings are in favor of a chronic exposure.

Our findings suggest weak correlation between BLL and electrophysiological abnormalities. Our findings are similar to Rubens *et al*.[3] and Thomson *et al*.,[4] studies that have reported no direct correlation between biochemical variables and clinical and electrophysiological data. However, Chen *et al*.[18] and Bordo *et al*.[19] have shown a significant decrease in NCV after a raised BLL. As mentioned above, it is likely that measurement of cumulative BLL can help in clarification of this relation.

Limitations of the study:

- Selecting control group from other department may be a limitation.
- It would be better If we had also compared the lower limb nerve conduction variables
- Data on environmental monitoring of lead exposre was not available

Table 4: Right radial nerve conduction study (mean (SD))

Investigated indices in nerves	Patient	Control group	*P* value
SNAP	23.32 (1.26)	25.83 (2.04)	0.000
PL	2.28 (0.27)	2.28 (0.08)	0.85
SNCV	42.75 (1.48)	43.90 (1.08)	0.025

SNAP=Sensory nerve action potential (µV); PL=Peak latency; SNCV=Sensory nerve conduction velocity

Table 5: Electrodiagnostic indices in which significant correlation with blood lead level was seen

Nerve Conduction Variables	*P* value	Pearson correlation
SNCV in left ulnar nerve	0.037	0.330
SNCV in left radial nerve	0.032	0.339
DML in right ulnar nerve	0.000	0.528
MCV in left median nerve	0.025	0.355
MCV in right ulnar nerve	0.026	0.353
MCV in left ulnar nerve	0.012	0.393

(SNCV)=Sensory nerve conduction velocity; (DML)=Distal motor latency; (MCV)=Motor conduction velocity

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