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Plasma Malondialdehyde Level and Vibration Perception Threshold in Non-exposed Subjects and Lead-exposed Battery Workers

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Lead is toxic to multiple organ systems and oxidative stress is one of the key mechanisms in lead toxicity. Long-term exposure can result in lead neuropathy, typically motor neuropathy. Peripheral sensory neuropathy caused by lead exposure is still controversial. The aim of this study was to determine and compare plasma malondialdehyde (MDA) level and vibration perception threshold (VPT) between non-exposed subjects and lead-exposed battery workers. This case-control analytical study included 28 non-exposed subjects and 28 lead-exposed battery workers of small-scale battery work-places in Insein and North Okkalapa townships. Plasma malondialdehyde level was determined by colorimetric method. The function of large myelinated peripheral sensory nerve fibers was determined by vibrometer and described as vibration perception threshold (VPT). The mean blood lead level of the lead-exposed battery workers (4.25±3.87 μg/dl) was significantly higher ($p=0.007$) than that of the non-exposed subjects (2.14± 1.02 μg/dl). The mean plasma MDA level of lead-exposed battery workers was significantly ($p<0.001$) higher than that of the non-exposed subjects and their plasma MDA levels were 2.08±0.94 μmol/l and 0.9±0.43 μmol/l, respectively. Both mean values of VPT (hand and foot) in the lead-exposed battery workers were significantly higher than that of non-exposed subjects ($p=0.002$). There was no significant correlation between plasma MDA level and VPT measurements in the lead-exposed battery workers. Therefore, lead-induced lipid peroxidation and early abnormality in peripheral sensory nerve function could occur in the lead-exposed battery workers even at the low blood lead level but there was no evidence in relationship between lead-induced lipid peroxidation and peripheral sensory nerve impairment in lead-exposed battery workers.

Key words: Lead, Oxidative stress, Plasma malondialdehyde, Vibration perception threshold

INTRODUCTION

Lead is a toxic metal and its widespread use has caused extensive environmental contamination and lead exposure is estimated to account for 0.6% of the global burden of disease, with the highest burden in developing regions.[1] In developed countries, due to better identification, monitoring, and improvement in industrial safety methods, occupational lead exposure has been significantly reduced. However, in developing countries, lead toxicity is a persistent health problem for occupational workers and lead-acid battery manufacturing plants are one of the leading sources of occupational lead poisoning.[2]

Lead potentially induces oxidative stress and lipid peroxidation in animal studies. Yiin and Lin found that blood lead concentration was positively associated with lipid peroxidation in workers exposed to lead.[3] Agency for Toxic Substances and Disease Registry (ATSDR) indicated that

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lead toxicity can affect every organ system and the nervous system is the most sensitive target of lead exposure.[4] Traditionally, the neuro-muscular disorder associated with lead poisoning has been purely motor neuropathy.[5] Peripheral sensory neuropathy caused by lead exposure is still controversial. The main pathological change in the peripheral nerve fibres consists of segmental demyelination and may be associated with pronounced slowing of nerve conduction velocity.[6] Sata, *et al*. suggested that fast nerve fibres which conduct vibration sense were sensitive to chronic exposure to lead.[7]

This study was undertaken to determine and compare plasma malondialdehyde (MDA) level and vibration perception threshold (VPT) between non-exposed subjects and lead-exposed battery workers and to find out the relationship between plasma MDA level and VPT of lead-exposed battery workers.

MATERIALS AND METHODS

This is a case-control analytical, one year study from April 2015 to February 2016. In this study, male participants were only recruited to avoid gender difference that was one of the confounding factors in determining the peripheral sensory neuropathy. Twenty-eight male workers from small-scale battery workplaces in Insein and North Okkalapa townships and another twenty-eight non-exposed male subjects from University of Medicine 1 (Yangon) were recruited. The age range of the participants was 20-45 years.

Written informed consent was obtained. Two milliliter of blood were withdrawn from ante-cubital vein under aseptic condition and collected in a test tube containing anticoagulant (EDTA) for plasma MDA assay. After centrifuge, plasma was kept in a plain test tube and plasma MDA was determined within 6 hours from time of sample collection. After the blood samples were collected, the subjects were asked to take sitting rest for 5 minutes and they were explained about the procedure for vibration perception threshold. The sites used in the measurements were the left and right index finger, the left and right big toes. The Yes/No method was used to find out whether the subject perceived the vibration sense or not. The vibration was increased gradually from the least minimum voltage and the transition from no vibration perception to the onset of perceiving vibration, i.e. when the subject sensed the vibration by the Yes was taken as vibration perception threshold (VPT). The test was repeated three times for each subject and the average was taken for analysis. The vibration perception threshold (VPT) was expressed in volts (V).[8]

Data were presented as mean±SD. Data analysis was done by using the Statistical Package for Social Sciences (SPSS) software version 16. This study was done according to Guideline of Board of Studies Physiology, University of Medicine 1, (Yangon).

RESULTS

The blood lead levels (BLL) were found to be significantly higher in the lead-exposed group compared to the control group (4.25±3.87 µg/dl *vs.* 2.14±1.02 µg/dl, p=0.007). Figure 1 shows that plasma MDA level in the lead-exposed group was significantly higher (2.08±0.94 µmol/l) when compared to the control group (0.9±0.43 µmol/l). Vibration perception threshold levels were significantly higher in lead-exposed workers than in controls (Fig. 2 & Fig. 3).

Table 1. Relationship between plasma malondialdehyde (MDA) level and vibration perception threshold (VPT) in the lead-exposed battery workers (n=28)

Correlation parameters	Pearson's correlation 'r'	p
MDA *vs*. VPT (hand)	0.018	0.928
MDA *vs*. VPT (foot)	0.094	0.635

The strength of the correlation between plasma MDA level and VPT of the lead-exposed battery workers are shown in Table 1.

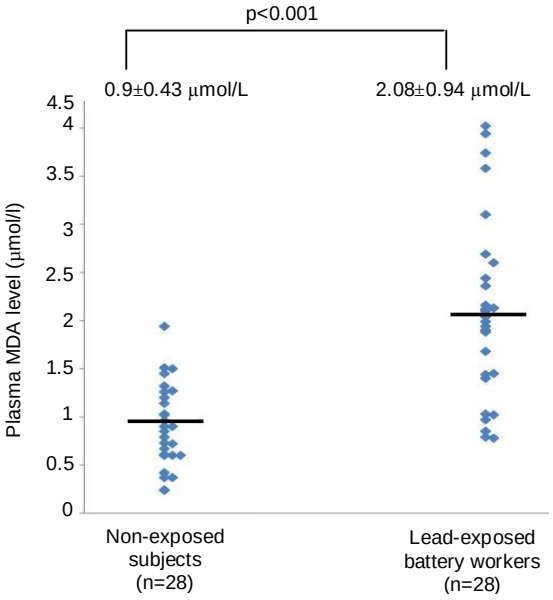

Fig. 1. Comparison of plasma malondialdehyde (MDA) level between the non-exposed subjects and lead-exposed battery workers (Solid line (—) indicates mean of different groups)

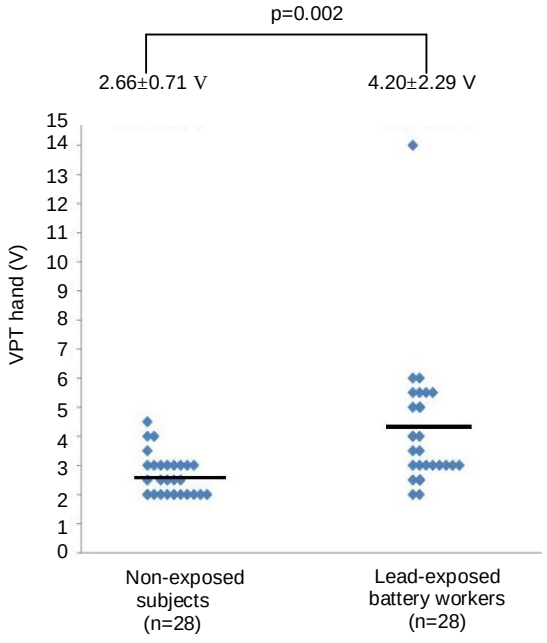

Fig. 2. Comparison of vibration perception threshold (VPT) (hand) between the non-exposed subjects and lead-exposed battery workers (Solid line (—) indicates mean of different groups)

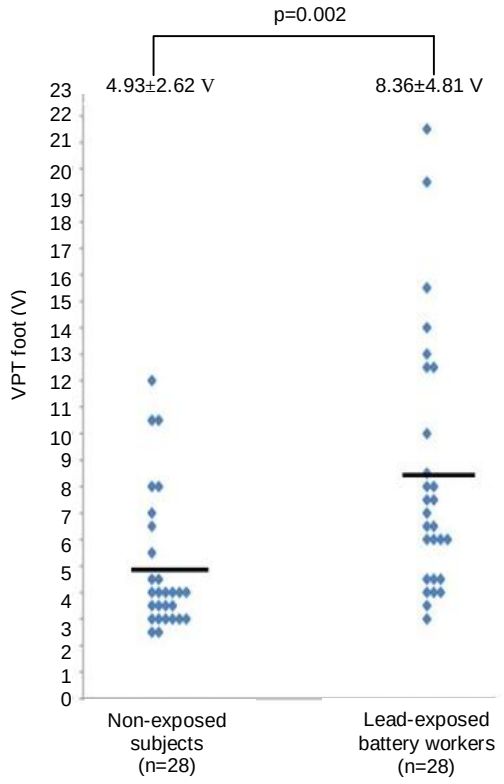

Fig. 3. Comparison of vibration perception threshold (VPT) (foot) between the non-exposed subjects and lead-exposed battery workers (Solid line (—) indicates mean of different groups)

DISCUSSION

Several lines of evidence have demonstrated that lead induces oxidative damage by inducing the generation of reactive oxygen species and by reducing the antioxidant cell defense systems.[9] Free radicals activity has been implicated in the pathogenesis of a variety of human diseases and the analysis of the data showed that oxidative stress was quite clear in lead-exposed workers (Fig. 1), as noticed by increased plasma MDA levels, which is in agreement with other studies.[10, 11]

According to the study of Nielsen and co-workers, the estimated reference range of plasma MDA level for male is from 0.39 to 1.53 µmol/l.[11] In this study, it was observed that plasma MDA level of the non-exposed subjects was within normal range, whereas only one subject of the non-

exposed group had higher MDA level than 1.53 μmol/l. Among the lead-exposed battery workers, 19 out of 28 subjects had plasma MDA levels higher than the upper limit of the estimated reference range of plasma MDA (1.53 μmol/l) and it indicated that higher lead exposure could generate more reactive oxygen species which lead to an increase in lipid peroxidation.

Most studies have reported that lead exposure causes oxidative stress by increasing lipid peroxidation.[4, 9, 10, 12] Although the findings of the this study are consistent with those results, the participants had lower blood lead level. Meanwhile, according to an invited critical review by Ahamed and Siddiqui, low level of lead exposure also induces oxidative stress.[13]

The classic description of lead neuropathy is that of a motor neuropathy, which typically presents as wrist drop.[14] More recently, investigators demonstrated that, in the development of lead neuropathy, sensory nerve fibers are affected earlier than motor nerve fibers.[14-16] Few studies have focused on peripheral nerve toxicity of lead with VPT changes.[15, 16]

In this study, as the participants' age group criterion was 20-45 years, the VPT cut-point based on VPT age-specific reference value for diagnosis of neuropathy was 15V.[5] Therefore, VPT ≤15 V indicated no neuropathy for our participants' age group. Although the mean VPT (hand) and mean VPT (foot) in both groups were within normal limit, the lead-exposed battery workers showed significantly higher VPT (hand) and VPT (foot) values than the non-exposed subjects. The most likely explanation for this finding is that sensory nerve conduction was slowed in battery workers and it might be due to myelin loss or axonal degeneration.[15] Whatever the underlying nerve pathology, there may seem to be a minimal conduction defect in the lead-exposed workers. The evidence we have obtained indicates that exposure to lead may give rise to peripheral sensory nerve fiber damage even at the low level of lead exposure.

These findings indicate no correlation between lipid peroxidation parameter and vibration perception threshold. There was limited evidence on effect of lead-induced lipid peroxidation on VPT measurements. Lead-induced neurotoxicity was found to be associated with lead-induced production of ROS which caused an increase in lipid peroxidation and the effects were concentration dependent.[3]

Lack of the correlation between the plasma MDA level and VPT in the lead-exposed battery workers might probably be due to either low lead level exposure or smaller sample size. It could be speculated that low lead level exposure might produce inadequate amount of ROS formation to initiate significant effect of lipid peroxidation on the large myelinated peripheral sensory fibers in the lead-exposed battery workers. Therefore, a large scale study with high-lead exposed subjects is recommended to confirm the relationship between lipid peroxidation and neuronal impairment.

Moreover, this study suggests that lead-exposed battery workers should have their peripheral nerve function examined carefully, including fast sensory nerve fibres. The VPT screening test is non-invasive, painless, and easy to perform in the field, and it has the potential to be developed for occupational physicians to screen for lead-induced peripheral sensory neuropathy at the workplace.

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