ORIGINAL ARTICLE

Comprehensive Electrocardiographic Analysis of Lead Exposed Workers: An Arrhythmic Risk Assessment Study

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Background: To evaluate electrocardiographic parameters which are related with atrial and ventricular arrhythmias measured from 12-lead surface electrocardiogram (ECG) in workers occupationally exposed to lead.

Methods: Sixty lead-exposed workers and 60 healthy controls were enrolled. Twelve-lead surface ECG was recorded and measurements of P wave durations (Pmax, Pmin) and P wave dispersion (PWD), QT durations and dispersion (QTd), corrected QT (QTc), Tp-e interval, and Tp-e/QT ratio were analyzed.

Results: The lead-exposed and control groups were similar with respect to baseline demographic, laboratory, and transthoracic echocardiographic indices. PWD (26.3 ± 9.7 vs 22.0 ± 9.0 ms, $P = 0.014$), Pmin (89.9 ± 13.8 vs 79.2 ± 10.1 ms, $P < 0.001$), and Pmax (116.2 ± 15.0 vs 101.2 ± 14.2 ms, $P < 0.001$), QT maximum (377.0 ± 27.6 vs 364.9 ± 28.5 ms, $P = 0.02$), QTd (38.4 ± 16.5 vs 30.5 ± 12.4 ms, $P = 0.004$), Tp-e interval (78.9 ± 16.5 vs 70.3 ± 14.5 ms, $P = 0.003$), and Tp-e/QT ratio (0.22 ± 0.04 vs 0.20 ± 0.04 , $P = 0.013$) were significantly higher in lead-exposed workers. QT minimum and QTc values did not differ significantly. QT maximum, QTd, and Tp-e/QT ratio were correlated with urine lead level and Tp-e interval was correlated with both blood and urine lead levels.

Conclusions: Lead-exposed workers have a higher risk for atrial and ventricular arrhythmias even without overt cardiac diseases compared with healthy subjects. These workers should be followed closely for adverse cardiovascular outcomes especially arrhythmias.

Ann Noninvasive Electrocardiol 2017;22(2):e12376, <https://doi.org/10.1111/anec.12376>

lead exposure; P wave dispersion; QT interval; Tp-e interval; Tp-e/QT ratio

Although the effects of heavy metal exposure are prevented effectively in daily life, occupational exposure to workers in production and chemical industries is still an important health problem.¹ One of them, lead is the most frequently encountered occupational and environmental heavy metal exposure in most countries. Although efforts have been made to reduce the emission of lead during work, occupational lead exposure is still a major concern in work places. Adverse effects of lead primarily involve the neuropsychiatric system, but effects to the cardiovascular

system have also been a topic of research in many studies.^{2,3} However, there are a few relevant studies investigating the effects of lead on the cardiac conduction system. In these studies, the relationship between lead exposure and electrocardiographic parameters such as QT interval, QRS duration and conduction disturbances have been investigated.⁴⁻⁶

QT dispersion (QTd), which is derived from 12-lead surface electrocardiogram (ECG), is the difference between the maximum and minimum QT interval. It is accepted as a simple and

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Conflict of Interest: None declared.

Source of funding: None.

© 2016 Wiley Periodicals, Inc.
DOI: 10.1111/anec.12376

noninvasive measurement of dispersion of ventricular repolarization and associated with arrhythmic events in various clinical settings.⁷ The Tp-e interval, which is the interval between the peak and the end of T wave on ECG, can be used as an index of total dispersion of repolarization.⁸ In addition, as a new index, the Tp-e/QT ratio, has been suggested to be a more accurate measure of dispersion of ventricular repolarization compared with QTd and Tp-e intervals alone.^{9,10} On the other hand, P wave dispersion (PWD), defined as the time difference between maximum and minimum duration of P waves on 12-lead ECG, is a noninvasive marker of disorganized atrial repolarization, and was proposed to be used as a predictor of atrial fibrillation.¹¹

Although conduction disturbances such as atrio- and intraventricular blocks and QT interval have been studied frequently in case of lead exposure, the effects of lead on the above-mentioned electrocardiographic parameters, as markers of atrial and ventricular arrhythmias, are not well known. The aim of this study was to evaluate electrocardiographic parameters, including QT interval, corrected QT (QTc), QTd, PWD, Tp-e interval and Tp-e/QT ratio, in workers occupationally exposed to lead and without clinical presentation of cardiac involvement.

METHODS

Study Population

In this cross-sectional study, demographic, clinical, laboratory, and electrocardiographic characteristics of 352 individuals presenting to our center between March 2014 and September 2015 were evaluated. All participants had a complete history taken and physical examination performed. Body mass index (BMI) was calculated as weight (kg)/height² (m). Blood pressure (BP) measurement was performed in each participant from the left arm following approximately 5 min of seated rest. Standardized mercury sphygmomanometers were used. Korotkoff phase I (appearance) and phase V (disappearance) sounds were recorded for systolic BP and diastolic BP, respectively. Twelve-lead surface ECG, laboratory, and transthoracic echocardiography findings were evaluated.

Workers with coronary artery disease, pre-existing hypertension (HT) defined as systolic BP >140 mmHg and diastolic BP >90 mmHg and/or

taking antihypertensive medication, valvular heart disease except trivial regurgitations, diabetes mellitus, thyroid dysfunction, hyperlipidemia, cigarette smokers, chronic lung disease, and bundle branch block or atrioventricular conduction abnormalities on ECG and ECGs without clearly analyzable P wave, QT, and Tp-e intervals were excluded from the study. All of the participants were in sinus rhythm and none of them were taking medications that can affect ECG such as antiarrhythmic drugs including beta-blocking agent and calcium channel blocker, tricyclic antidepressants, and antipsychotics. After taking into account these exclusion criteria, 292 participants were excluded and the study was carried out with a total of 60 patients. Among them, 16 (27.0%) were involved in battery production, 25 (41.6%) were involved in metal recycling, 7 (11.6%) were welders, and 12 (20.0%) were involved in metal production.

All of the workers worked for 5 days a week and 8 hours a day. Most of the work places that the workers worked in were small- and medium-sized enterprises. Therefore, in most of these work places, measurement of environmental exposure/toxic substance was not done. In the small number of work places where measurements were done, accurate values could not be obtained because of incorrect measurements and inadequate data. Sixty healthy controls who worked in our center as hospital staff without known overt cardiovascular disease matched for age and gender served as the control group. All study population was over the age of 18 years and men. Written informed consent was obtained from each subject and the institutional ethics committee approved the study protocol.

Collection of Biological Samples and Analysis Methods

Blood samples were taken from the workers at end of work shift. Blood samples were drawn in 10 mm tubes with red caps not containing gel (BD Vacutainer) for the analysis of biochemical parameters. For serum analyses, the specimens were centrifuged at 1500×g for 10 min after at least 30 min of incubation. All samples were analyzed on the same day. Lead levels were determined in whole blood and 24-hour urine samples using Inductively Coupled Plasma Mass Spectrometry (Agilent 7700 series, Tokyo, Japan). Blood samples were digested by the microwave-induced acid

digestion method. Standard solution of lead was prepared by dilution of certified standard solutions (High Purity Standards, Charleston, SC, USA). Two-level quality control materials were used (Seronorm, Billingstad, Norway). The lead calibration curve ranged from 0 to 100 µg/dL. Limit of detection and Limit of quantification were 0.02 and 0.1 µg/dL, respectively. % Relative Standard deviation of measurements was 4.2. Subjects were asked to collect 24-hour urine samples. They were instructed not to collect urine from the first urination after waking on the morning of the day they started to collect the urine. Urine samples were collected in sterile plastic pots thereafter, including the first urination upon waking the following morning, and then diluted 1 in 10 with 5% nitric acid solution.

Electrocardiography

Twelve-lead surface ECG was recorded at a paper speed of 50 mm/s (Nihon Kohden, Tokyo, Japan) at rest in supine position and at the same time as subjects blood lead measurements were extracted. The following ECG features were studied by a cardiologist who was blind to the participant data and verified by a second physician to avoid any error in measurements: Resting heart rate (HR), maximum and minimum P wave duration, PWD, maximum and minimum QT interval, QTc, QTd, Tp-e interval, and Tp-e/QT ratio.

Resting HR was measured from ECG taken during subject evaluation. P wave duration was measured manually. The onset of P wave was defined as the point of first visible upward slope from baseline for positive waveforms, and as the point of first downward slope from baseline for negative waveforms. The return to baseline was considered the end of P wave. The maximum and minimum durations of P waves (P max and P min, respectively) were calculated, and the difference between P max and P min was defined as PWD (PWD = P max – P min).¹²

The QT interval was measured manually from the onset of the QRS complex to the point at which the tangent of the maximal down slope of the descending limb of the T wave crossed the isoelectric baseline. If U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. Maximum QT (QT max) and minimum QT (QT min) were calculated. Dispersion parameters were calculated as

the difference between the maximal and minimal values of QT. QT interval was corrected for HR using the Bazett formula: $QT_c = QT/\sqrt{R-R}$ interval.¹³ The Tp-e interval was defined as the interval from the peak of T wave to the end of T wave. Measurements of Tp-e interval were performed from precordial leads.¹⁴ Finally, the Tp-e/QT ratio was calculated from these measurements. Intra- and interobserver variability were 4.2% and 4.9%, respectively.

Transthoracic Echocardiography

Standard echocardiographic imaging was performed in the left lateral decubitus position with the ESAOTE cardiac ultrasound scanner (Indianapolis, IN, USA). Images were obtained using a 2.5–3.5 MHz transducer in the parasternal and apical views. Left ventricular end-diastolic (LVEDD) and left ventricular end end-systolic (LVESD) diameters were determined with M-mode echocardiography under two-dimensional guidance in the parasternal long-axis view, according to the recommendations of the American Society of Echocardiography.¹⁵ LVEDD and LVESD diameters were determined with M-mode echocardiography under two-dimensional guidance in the parasternal long-axis view. Left ventricular (LV) endocardial borders were manually traced at end-diastole and end-systole in the apical four- and two-chamber views and left ventricular ejection fraction (LVEF) was calculated according to the modified biplane Simpsons rule. In cases where the Simpsons method could not be used, LVEF was calculated using the Teicholz method. In addition, left atrial dimension in parasternal long-axis view and right ventricular end-diastolic diameter in apical four-chamber view were also calculated. Pulmonary systolic arterial pressure (sPAP) was estimated by continuous-wave Doppler as peak regurgitation velocity plus an assumed right atrial pressure in relation to the size and respiratory excursion of inferior cava vein visualized in subcostal view. Mitral inflow velocities were measured by pulsed wave Doppler from the apical four-chamber view positioned at the tips of the mitral leaflets at end expiration. The peak early filling velocity (E wave), peak filling velocity during atrial systole (A wave), the E/A ratio, and the deceleration time of the early filling velocity were calculated. The isovolumic relaxation time was derived using

pulsed wave Doppler by placing the cursor in the LV outflow and mitral inflow simultaneously and recorded as time interval between aortic valve closure and mitral valve opening.

Statistical Analysis

Statistical evaluation was performed using Statistical Package for Social Sciences (SPSS 20) for Windows (IBM SPSS Inc., Chicago, IL, USA). Variables with normal distribution were analyzed using Kolmogorov-Smirnov test. Variables with normal distribution were shown as mean $\pm$ standard deviation, whereas those without normal distribution were shown as median with minimum and maximum range. Categorical variables were shown as number and percentage. Comparison between groups of continuous variables was performed with *t*-test for independent variables showing normal distribution and Mann-Whitney U test for those not showing normal distribution. Pearson correlation analysis was used to test normal distribution, whereas Spearman correlation analysis was used for variables not showing normal distribution. $P < 0.05$ was considered statistically significant. Multiple linear regression analysis was used to determine predictors among risk factors thought to be related to electrocardiographic parameters in lead-exposed group.

RESULTS

General Characteristics of Study Population

The baseline demographic, clinical, and echocardiographic parameters of the lead-exposed group and the control group are presented in Table 1. No significant difference was present between the groups in terms of age, BMI, HR, systolic and diastolic BP values, and all of echocardiographic findings. All the participants of the two groups were males. The mean age of the lead-exposed group was 37.2 ± 8.0 years and that of the control group was 38.3 ± 9.0 years ($P = 0.488$). Participants of both groups were overweight according to BMI (26.0 ± 3.7 kg/m² for lead exposed and 25.1 ± 3.6 kg/m² for control group, $P = 0.183$). The HR of the lead-exposed group was 72.8 ± 12.1 bpm and that of the control group was 71.5 ± 11.1 bpm. The LVEF of the two groups was similar (65.4% for lead-exposed group and 64.4% for control group).

The complete blood count and biochemical parameters are shown in Table 2. Hemoglobin, white blood cell and platelet counts, neutrophil count, erythrocyte sedimentation rate and C-reactive protein levels, creatinine, fasting blood glucose, alanine aminotransferase,

Table 1. Demographic Characteristics, Blood Pressure, and Echocardiographic Parameters of the Lead-exposed and Control Groups

Variables	Lead-exposure Group (n = 60)	Control Group (n = 60)	P Value
Age (year)	37.2 ± 8.0	38.3 ± 9.0	0.488
BMI (kg/m ²)	26.0 ± 3.7	25.1 ± 3.6	0.183
Heart rate (/bpm)	72.8 ± 12.1	71.5 ± 11.1	0.547
Systolic BP (mmHg)	120.0 ± 13.7	119.8 ± 11.3	0.925
Diastolic BP (mmHg)	74.1 ± 9.8	71.0 ± 8.2	0.068
End-diastolic diameter (mm)	45.6 ± 3.0	46.0 ± 3.0	0.467
End-systolic diameter (mm)	27.1 ± 3.5	28.2 ± 3.3	0.088
LVEF (%)	65.4 ± 2.9	64.4 ± 3.8	0.125
sPAP (mmHg)	23.4 ± 4.8	22.8 ± 3.9	0.453
RV diameter (mm)	25.3 ± 2.3	25.8 ± 3.3	0.338
Left atrium diameter (mm)	33.9 ± 4.0	33.7 ± 4.8	0.758
E wave (cm/s)	81.2 ± 15.8	79.3 ± 14.9	0.499
A wave (cm/s)	65.8 ± 12.6	66.5 ± 13.6	0.77
DT (ms)	179.1 ± 43.6	178.4 ± 44.2	0.93
IVRT (ms)	88.4 ± 13.9	92.3 ± 15.0	0.142

BP = blood pressure; BMI = body mass index DT = deceleration time; IVRT = isovolumic relaxation time; LVEF = left ventricular ejection fraction; RV = right ventricle; sPAP = systolic pulmonary arterial pressure.

aspartate aminotransferase, uric acid, and blood urea nitrogen were similar in the two groups ($P > 0.05$). The median blood lead level was $33.9 \mu\text{g/dL}$ (minimum 4.9 and maximum $90 \mu\text{g/dL}$) in the lead-exposed group and $0.3 \mu\text{g/dL}$ (minimum 0.1 and maximum $1.0 \mu\text{g/dL}$) in the control group. The median 24-hour urine lead level was $33.7 \mu\text{g/L}$ (minimum 2 and maximum 292) in the lead-exposed group and $0.7 \mu\text{g/L}$ (minimum 0.1 and maximum 1.5) in the control group.

Electrocardiographic Parameters

The parameters derived from 12-lead surface ECG are shown in Table 3. Significant difference was

present between the lead-exposed group and the control group in terms of PWD ($26.3 \pm 9.7 \text{ ms}$ vs $22.0 \pm 9.0 \text{ ms}$, $P = 0.014$), P_{max} ($116.2 \pm 15.0 \text{ ms}$ vs $101.2 \pm 14.2 \text{ ms}$, $P < 0.001$), P_{min} ($89.9 \pm 13.8 \text{ ms}$ vs $79.2 \pm 10.1 \text{ ms}$, $P < 0.001$), QT_{max} ($377.0 \pm 27.6 \text{ ms}$ vs $364.9 \pm 28.5 \text{ ms}$, $P = 0.02$), QT_d ($38.4 \pm 16.5 \text{ ms}$ vs $30.5 \pm 12.4 \text{ ms}$, $P = 0.004$), $Tp\text{-}e$ interval ($78.9 \pm 16.5 \text{ ms}$ vs $70.3 \pm 14.5 \text{ ms}$, $P = 0.003$), and $Tp\text{-}e/QT$ ratio (0.22 ± 0.04 vs 0.20 ± 0.04 , $P = 0.013$). However, QT_{min} and QT_c values did not differ significantly.

In univariate correlation analysis in the lead exposure group, urine lead level was found to be correlated with QT maximum ($r = 0.267$, $P = 0.039$, Fig. 1A), QT_d ($r = 0.271$, $P = 0.036$,

Table 2. Laboratory and Serologic Data of the Lead-exposed and Control Groups

Variables	Lead-exposed Group (n = 60)	Control Group (n = 60)	P Value
Hemoglobin (g/dL)	14.7 ± 1.3	14.9 ± 2.7	0.643
White blood cell ($/\mu\text{L}$)	7791 ± 1815	7545 ± 1611	0.433
Platelet count ($/\mu\text{L}$)	$236,866 \pm 59,665$	$254,677 \pm 48,416$	0.114
Neutrophil count ($/\mu\text{L}$)	4608 ± 1478	4572 ± 1058	0.877
ESR (mm/hour)	2.5 (2–32)	2.0 (2–25)	0.671
CRP (mg/dL)	2.3 (1–12)	2.0 (2–8)	0.524
Creatinine (mg/dL)	0.78 ± 0.15	0.82 ± 0.21	0.232
Fasting glucose (mg/dL)	92 (76–113)	88 (75–100)	0.466
ALT (U/L)	20.0 (5–77)	18 (5–42)	0.348
AST (U/L)	19.5 (11–37)	18.0 (7–32)	0.405
Uric acid (mg/dL)	5.62 ± 1.18	5.28 ± 1.5	0.17
BUN (mg/dL)	13.9 ± 3.5	13.1 ± 3.2	0.182
Lead/blood ($\mu\text{g/dL}$)	33.9 (4.9–90)	0.3 (0.1–1.0)	<0.001*
Lead/urine ($\mu\text{g/dL}$)	33.7 (2–621)	0.7 (0.1–1.5)	<0.001*

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

* statistical significance

Table 3. Electrocardiographic Parameters of the Lead-exposed and Control Groups

Variables	Lead-exposed Group (n = 60)	Control Group (n = 60)	P Value
P minimum (ms)	89.9 ± 13.8	79.2 ± 10.1	0.001
P maximum (ms)	116.2 ± 15.0	101.2 ± 14.2	0.001
PWD (ms)	26.3 ± 9.7	22.0 ± 9.0	0.014
QT minimum (ms)	338.3 ± 22.9	334.4 ± 27.2	0.39
QT maximum (ms)	377.0 ± 27.6	364.9 ± 28.5	0.02
QT_d (ms)	38.4 ± 16.5	30.5 ± 12.4	0.004
QT_c (ms)	349.6 ± 27.1	357.6 ± 23.9	0.089
$Tp\text{-}e$ interval (ms)	78.9 ± 16.5	70.3 ± 14.5	0.003
$Tp\text{-}e/QT$ ratio	0.22 ± 0.04	0.20 ± 0.04	0.013

QT_d = QT dispersion; QT_c = corrected QT; PWD = P wave dispersion.

Table 4. Univariate Correlation Analyses Findings between Blood and Urine Lead Levels and Electrocardiographic Parameters in the Lead-Exposed Group

Variables	Blood Lead Level (µg/dL)		Urine Lead Level (µg/L)	
	r	P	r	P
P minimum (ms)	−0.060	0.647	0.026	0.846
P maximum (ms)	−0.035	0.790	0.104	0.430
PWD (ms)	0.040	0.761	0.159	0.225
QT minimum (ms)	−0.112	0.393	0.172	0.190
QT maximum (ms)	0.121	0.356	0.267	0.039
QTd (ms)	0.086	0.516	0.271	0.036
QTc (ms)	0.111	0.397	0.232	0.075
Tp-e interval (ms)	0.310	0.016	0.450	0.001
Tp-e/QT ratio	0.254	0.050	0.377	0.003

QTd = QT dispersion; QTc = corrected QT; PWD = P wave dispersion.

Fig. 1B), Tp-e interval ($r = 0.450$, $P = 0.001$, Fig. 2A), and Tp-e/QT ratio ($r = 0.377$, $P = 0.003$, Fig. 2B), significantly. In addition, blood lead level was only found to be correlated with Tp-e interval significantly ($r = 0.310$, $P = 0.016$). Multivariate stepwise linear regression model was used to determine possible independent predictors that may be effect all electrocardiographic parameters, but none of the baseline clinical, laboratory, or echocardiographic parameters were found to be

independent predictors of these electrocardiographic parameters.

DISCUSSION

The main findings of this study are as follows: (1) Pmin, Pmax, PWD, QTmax, QTd, Tp-e interval, and Tp-e/QT ratio were prolonged in lead-exposed group compared with that of the controls; and (2) QT maximum, QTd, and Tp-e/QT ratio were significantly and positively correlated with urine lead level and Tp-e interval was significantly and positively correlated with both blood and urine lead levels. However, other electrocardiographic parameters including QT minimum and QTc did not differ between the lead exposure and control groups.

Increased risk of cardiovascular morbidity and mortality has been demonstrated in lead-exposed individuals.³ Although many studies have documented that lead exposure is associated with ischemic heart disease,¹⁶ HT,^{17,18} and cerebrovascular accident,¹⁹ cardiac conduction tissue can also be affected leading to conduction abnormalities and arrhythmias. In a study from Taiwan, Chen et al.⁶ found that workers exposed to lead occupationally had significantly shorter PR interval and longer QTc interval compared with controls. Furthermore, no significant relationship of blood lead level was observed with PR interval,

Figure 1. In the lead-exposed group, correlation between 24-hour urine lead level and maximum QT duration (A) and QT dispersion (B).

Figure 2. In the lead-exposed group, correlation between 24-hour urine lead level and Tp-e interval (A) and Tp-e/QT ratio (B).

whereas there was a significant relationship with QTc. In another study, long-term lead exposure in nonoccupational cohort as measured in bone lead was associated with prolonged QTc and JT intervals and QRS duration.²⁰

Studies related to lead exposure have included only limited electrocardiographic parameters. In this study, indicators of both atrial and ventricular arrhythmias were studied comprehensively. P wave durations such as Pmin, Pmax, and PWD were evaluated as indicators of atrial arrhythmias, and QTmin, QTmax, QTd, and QTc were evaluated as indicators of ventricular conduction and possible ventricular arrhythmias. Besides, Tp-e interval and Tp-e/QT ratio, both of which are popular in recent years in electrophysiology as indicators of ventricular conduction system, have also been evaluated. Apart from QTmin and QTc, all other parameters were significantly higher in the lead-exposed group. By which mechanisms does lead causes such detrimental effects on the atrial and ventricular conduction system? Firstly, effects of lead on calcium homeostasis may play an important role. Blunted calcium homeostasis caused by leads resemblance to this ion inevitably disrupts cardiac messenger system.⁴ Secondly, increased sympathetic system activity that can be seen in lead exposure²¹ can trigger excitability of cardiac connecting tissue and lead to arrhythmias. In addition, there are some studies suggesting that

lead decreases the action of the parasympathetic system.^{22,23} Thus, sympatho-vagal imbalance emerges as an important mechanism of lead-related outcomes. The study of Poreba et al. supported this hypothesis. They found that decreased heart rate variability and abnormal heart rate turbulence, indices which are established noninvasive tools for prediction of arrhythmias, were more frequent in workers occupationally exposed to leads.⁵ Direct or oxidative stress-related cardiac tissue damage²⁴ may also cause structural and/or electrical heterogeneity. However, lead-related electrocardiographic changes are still not well understood. In addition, many studies have shown that lead induces oxidative stress by increasing the production of reactive oxygen species (ROS).²⁵ ROS so formed precipitate an inflammatory process by causing cell membrane damage via lipid peroxidation.²⁶ On the one hand, lead causes cellular damage and inflammation by increasing ROS via several pathways, whereas on the other hand the inflammation so triggered reinforces oxidative stress by positive feedback and potentializes the adverse effects of lead. Therefore, it is believed that the detrimental effects of lead are mediated by inflammation and oxidative stress.²⁷

In this study, the only parameter that correlated with blood lead level was Tp-e interval. However, urine lead level was found to be

correlated with not only Tp-e interval but also QT max, QTd, and Tp-e interval. In The Normative Aging Study, none of the electrocardiographic parameters were associated with blood lead levels, but increased bone lead level was associated with prolonged QTc, QRS duration, and increased risk of intra- and atrioventricular conduction abnormalities.⁴ The reason why blood lead level does not correlate with this parameters is that blood lead level reflects only relatively recent exposure but not the actual severity of chronic lead exposure. Urine lead level may reflect the long-term exposure and late effects of exposure on several systems of the body. Therefore, blood lead level may not be a strong indicator for abnormalities of the atrial and ventricular conduction system.

There are several limitations in this study. First of all, lead level has been studied only in blood and urine. Level of lead in bone has not been taken into account. About 95% of lead in the body is deposited in bones and lead in bone may better predict long-term lead toxicity than blood and urine lead level.²⁸ Secondly, because of the cross-sectional design of this study, follow-up of the patients is not present and no cardiovascular or arrhythmic end points have been defined. Therefore, interpretation of the long-term cardiovascular effects of lead with findings of this study is difficult. Exclusion criteria have been defined to nullify the effects of confounding parameters. Thus, the study group represents only a homogeneous group and is far from reflecting real-life. Because of this reason, the study was carried out with a very small population. This study has primarily been designed on exposed population. Those subjected to exposure has not been studied and analysis of measurements of work place environment has not been performed. Similarly, the effect of different sectors (like metal recycling, production, welding) has not been taken into account.

As a conclusion, this study showed that there were significant differences in various electrocardiographic parameters used as noninvasive tools for predicting atrial and ventricular arrhythmias in workers occupationally exposed to lead when compared with the healthy subjects. When the prognostic significance of these electrocardiographic parameters is considered, lead-exposed individuals should be followed closely for adverse cardiovascular outcomes, especially for arrhythmias.

However, larger and experimental trials are required to understand the pathogenesis of lead toxicity and to put light into specific treatments.

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