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STUDY OF A POPULATION OF GLASS CERAMIC WORKERS WITH POSSIBLE CHRONIC KIDNEY DAMAGE DUE TO TOXIC POISONING

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ABSTRACT

A sample was studied of the population possibly exposed to lead (Pb) due to their employment in ceramic glass. Of a very heterogeneous population, 219 workers interviewed and 129 workers selected for study participation. Who due to their on-the-job seniority, susceptibility and type of work that they carried out, suspected of having been exposure to Pb. Average Pb in blood was 17.4 ± 14.2 µg/dl, with a minimal value of 0.5 and maximal of 59.6 µg/dl. The 58% of the population analyzed was found with high Pb absorption magnitude with Blood Pb (BPb) >15 µg/dl, including 12% of workers >40 µg/dl. Average gamma-AminoLevulinic Acid Dehydratase (δ–ALAD) enzyme activity in blood, as a specific indicador of chronic Pb-associated damage, was 379 (nmoles)/ml/h of blood, finding 57.3% of workers with high Pb-related toxicity, reflecting that there are Pb accumulation and redistribution phenomena, given the chronic exposure. Data found in workers of oxidative damage in blood, alterations in neuromuscular behavior and motor coordination, and subclinical and clinical data compatible with exposure to and damage due to Pb. In addition, clinical data of Pb poisoning, proteinuria and persistent albuminuria found in 20% of the workers, indicating possible chronic kidney disease.

KEYWORDS Lead, glass ceramic, chronic kidney, AminoLevulinic Dehydratase

Introduction

Lead (Pb) is a metal that is widely utilized in multiple industries that identified as a toxin for exposed workers [1-5] Pb can contaminate work environments with distinct forms of exposure and from different compounds, which will exert an influence on their absorption form and absorption[4,5]. This metal can be absorbed by the respiratory and the digestive pathway depending on the type of exposure, the compound, and the manner in which it enters the organism (powders, smoke, vapors, gases, or particles, and by its presence in water, foods, or eating utensils)[1–3] . Once it enters the organism, Pb into the blood where it is distributed and redistributed to the remainder of the organs and tissues, reaching diverse equilibria that depend on the absorption and excretion, with a great tendency toward accumulation [4–6,11-13]. The entry of Pb into the different organs gives rise to damage in the cells that make them up [11]. Damage in the organism can range from moderate and local toxicity to generalized intoxication and even death [5,10,11]. The effects that Pb exerts depend on the amount that enters into the organism, the physiological and nutritional conditions, and the genetic predisposition of the worker. Therefore, it is not easy to associate PB-caused damage (amount of Pb and time of exposure), with the concentration of Pb in the blood or in damaged organ in particular [12,13,15]. The most utilized absorption and damage indicador is Pb concentration in blood; however, this determination is far from being the best indicador, due to the accumulation and redistribution of Pb, including its tendency to accumulate in bone [9, 13, 14]. There are also specific and early indicators of damage, such as the determination of *delta*-AminoLevulinic Dehydratase (δ–ALAD) enzymatic activity. The products of oxidation such as Thiobarbituric Acid Reactive Species (TBARS) [10,15,18] and physiological tests of neuromuscular behavior [4,5] these tests complement the information supplied by the evaluation of Pb in blood and allow to know the intensity of the problem and to define the initiation of toxic processes years prior to clinical manifestation of the intoxication. From the beginning of the toxic process, the Quality Of Life (QOL) of patients exposed to PB is notable reduced. In the particular case of the workers, their work efficiency also reduced and their absenteeism, collateral diseases, and their appointments with the physician increased. concentration of the worker diminishes, self-medication is generated, all these with increases in insurance costs, medical expenditures, and insurance rates, giving rise to great losses to the industry and elevating the risk of the presentation of lawsuits by the worker for partial or permanent damage due to labor risks and occupational diseases [1,3, 13,18,19]. The latter is in contrast with the relative ease of control of the contaminant processes that, with moderate investments, efficient personnel safety, and worker information systems, can avoid exposure to intoxication.

Working in the glass ceramics/glassworks industry is an activity that, in Dolores Hidalgo, Guanajuato, Mexico, carried out at the small-industry and home-industry levels and that represents the most important economic activity, including up to 54.3% of the economically active population. This activity implies, the majority of times, the use of different materials that contain Pb and that can contaminate the work environment with Pb salts, can be absorbed by and that can cause damage to the workers. Lead (Pb), as a toxic metal, can give rise in the long term to kidney damage in intoxicated workers. It has been documented that individuals with high serum levels of Pb present renal insufficiency and a Glomerular Filtration Rate (GFR) of <60 ml/min. The Pb that binds to Low-Molecular-Weight (LMW) proteins (<1% of the total) filters freely through the glomerular and is reabsorbed by the cells of the Convoluted Proximal Tubule (CPT) through endocytosis. It proven that, at the interior of the cell, and specifically in the mitochondria, damage in the respiratory chain, with an increase in Free Radicals (FR), a depletion of Glutathione (GSH), and apoptosis. Additionally, the enzymatic reactions in which calcium participate can be activated by Pb, which could explain the nephrotoxicity.

The Ministry of Health of the State of Guanajuato [7-9,16,17] has found that the frequency of patients with chronic kidney damage without antecedents of diabetes registered from 1999 to 2010 comprises fewer than 40,000 new cases annually as kidney failure (insufficiency), that is, an annual increase of 11%, which duplicated the increase observed previously. The State of Guanajuato registered nearly 604 cases (INEGI, 2010), with the Dolores Hidalgo Municipality that which increased from four to >24 cases/year at the Consultation Service of the Dolores Hidalgo General Hospital, accumulating 146 patients during those 10

years. Due to these reasons, this work evaluated the incidence and magnitude of Pb poisoning in a population sample of glass ceramic workers, as well as the association that this intoxication can have with the increase of cases of chronic kidney damage in this population.

Methods

Selection of the population

We evaluated a population of the Dolores Hidalgo Municipality, Guanajuato State, Mexico. Which was suspected of being occupationally exposed to Pb due to their work in glass ceramics: the universe of the population devoted to glass ceramic work is 70,000 (54.3%) of a total of 128,924 municipal inhabitants, according to Mexican National Institute of Statistics and Geography (INEGI) 2004 census data. The number of workers registered in the Association of Glass Ceramic Workers is only 365. After an informative meeting that emitted a summons to the 40 companies making up the Association, a positive response was obtained from 23 companies, with which an initial contact was carried out with 219 workers (60% of those registered), all of whom accepted to participate in the study. We applied to this group of study participants a questionnaire where workers were selected who had antecedents of exposure to Pb of >1 year, with occupational posts of greatest exposure (paint and enamel management, contact with contaminated powders) and who had mentioned possible damage to the renal system. The result was a sample of 129 workers (35% of employees registered in the Association of Glass Ceramic Workers). We explained, in the first instance, what the investigation comprised and asked the participants to sign a setter of informed consent for the studies, committing to confidentiality of information and the timely delivery of results individually.

Base of comparison with the Mexican Official Norm

The results contained from the concentration of BPb in the studied sample were classified based on the Mexican Official Norm (NOM-199-SSA1-2000) [14]: Category I.- BPb should not exceed 10 micrograms per 100 ml of blood [µg/dl]. Category II. - 10 and 14 µg/dl. Category III. - 15 and 24 µg/dl. Category IV. - 25 and 44 µg/dl. Category V. - 45 and 69 µg/dl and Category VI. - Concentrations >70 µg/dl.

Blood lead concentration

Lead concentration in blood determined by voltammetry with a Lead Analyzer, 3010B model (ESA). Determinations were in triplicate; standard curves calculated with the method of addition to minimize the matrix effect on the absorption peak (recovery of 85–113%). Precision of analyses was around 87–104% (using ESA Hi and Lo calibrators) and detection limit was one □g/dl. Concentration reported as □g of lead per dl of blood [18,19].

δ– ALAD activity used as a marker of lead poisoning

Erythrocyte δ–ALAD activity was determined spectrophoto metrically (UV/VIS DU 650; (Beckman) using the European standardized method as described by Berlin and Schaller. The enzyme activity expressed as nmoles of PorphoBilinoGen (PBG) per h per ml of erythrocytes (nmoles/h/ml) [15,18].

Lipid peroxidation is a biological marker of oxidative cellular damage

The amount of lipid peroxidation of the erythrocytes estimated as reported in Rendón Ramírez et al. (2013) by measuring the thiobarbituric acid-reactive substances (TBARS). Absorbance measured at 532 nm and 600 nm using an UV/VIS DU 650 spectrophotometer (Beckman). TBARS expressed as nmoles of malondialdehyde equivalents per ml of erythrocytes (nmoles/ml) [10].

Urinary proteinuria

The urine samples corresponded to the first urine of the day of the sample taking. These samples placed under refrigeration until their analysis in the laboratory, where they analyzed for diverse parameters, among which protein iin urine analyzed with reactive strips was included. Cases that resulted positive again analyzed in the clinical laboratory.

Results and Discussion

Blood Lead Concentration

The average age of the workers in the sample was 30 years (range, 13–74 years). Time of working in activities with possible lead exposure was 127 months on average, with a range of 4–600 months.

The BPb concentration obtained by voltammetry of the sample studied was 17.41 ± 14.1 µg/dl, with a minimal value of 0.5 and a maximal value of 59.6 µg/dl. Thirty one percent of the population analyzed placed in Category I, 31%; Category II, 11%; Category III, 26%; Category IV, 20% and 12% in Category V. The latter result in that 58% of the population analyzed is found within an elevated magnitude of lead absorption (Categories III, IV, and V), and this should be considered as a public health problem. It is noteworthy that 12% of the population considered in Category V, which already represents very high lead absorption (See Figure 1).

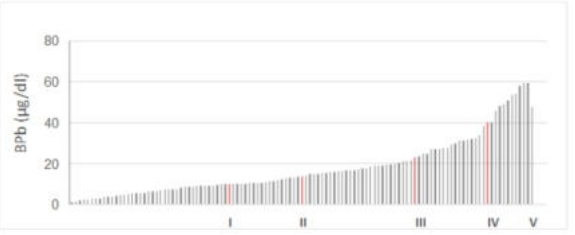

Figure 1. Distribution of Blood lead (BPb) concentration in glass ceramic workers, according to the categories of Mexican NOM-199-SSA1-2000

The workers classified in Category I, according to BPb concentration, are aged on average 35 years and with 153 months working in the possibly Pb-contaminated environment; workers classified in Category II were aged 32 years on average and had worked for 170 months. In Category III, workers were aged on average 28 years and had worked for 83 months, while in Category IV, workers were aged 24 years on average and had worked 101 months, and in Category V, average worker age was 20.6 years and they has worked in a possibly Pb-contaminated environment for 56.6 months, respectively.

The latter indicates that there can have been great lead absorption, although in young persons and in workers with little exposure time, and that these should be presenting phenomena of redistribution and defenses of workers exposed to lead for extended periods

Biochemical Lead Damage (Specific)

Average delta-AminoLevulinic Acid Dehydratase (δ–ALAD) enzyme in blood as a specific indicador of chronic lead damage was 382.77 nmoles/h/ml of blood, finding minimal values of 51 nm/h/ml of blood and maximal values of 1,312 nmoles/h/ml of blood. Workers (25.6%) with <600 nmoles/h/ml can be considered with low lead poisoning, and 57.3% of workers have high lead poisoning, with only 17.1% of workers with normal values of the activity (see Figure 2).

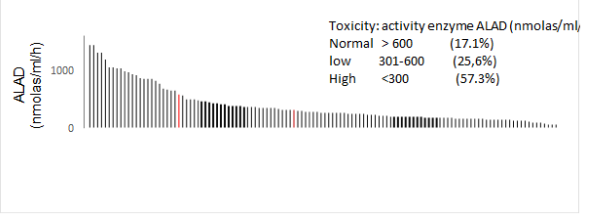

Figure 2. Distribution of δ-ALAD enzyme activity in blood of glass ceramic workers.

Changes in the activity of the enzyme coincides with the BPb concentration in the workers, with high toxicity (<300 of activity)

have an average BPb concentration of 22.8 µg/dl, and those with low toxicity (300–600 of activity) have an average of 11.3 µg/dl of lead. In contrast, workers with normal enzymatic activity (>600) have an average concentration of 9.0 µg/dl. These results associate toxicity with the lead concentration in different groups and indicate a subclinical lead-related intoxication process in the population.

Lead Damage (Nonspecific)

Oxidative damage in blood evaluated by means of the TBARS that form after oxidative damage to lipids. In the workers, the average was 1.33 nm/ml, with a minimum of 0.33 nm/ml and a maximum of 1.94 nm/ml. This correlated with the damage shown by the reduction of gamma-AminoLevulinic Acid Dehydratase (δ–ALAD) activity and the increase in the BPb concentration of the workers and contrasted with the oxidative damage found in populations without exposure to lead and that are clinically healthy, which is 0.85 nm/ml, according our studies in distinct populations. The latter indicates that all of the workers present oxidative damage considered as moderate-to-severe, showing chronic oxidative damage.

Chronic Kidney Damage

The results of the urine examinations permitted the identification of 26 workers (20.2%) who present proteinuria and albuminuria, which identifies them as patients with possible chronic kidney damage, which correlates with a greater BPb concentration of the patients. In patients with proteinuria (protein in urine >1 mg/dl), these were distributed with the following percentages based on classification categories by BPb concentration: Category I, 26.3%; Category II, 14.3%; Category III, 18%; Category IV, 23%, and Category V, with 37.5% (Figure 3). Urine analyses also showed a high frequency (41%; 40 workers) of urinary infections in the workers studied, which renders it possible for this to be related with lead exposure or some other work factor that cannot be identified in the study. The incidence of proteinuria and microalbuminuria in open population is about 5% (20). As can be observed in the sample of workers possibly exposed to Pb, the incidence is 20%, indicating a notable increase and that demonstrates that the incidence is not a populational finding, but rather that there must be factors that induce chronic kidney damage, with exposure ot lead a primordial factor. Additionally, it was found that workers with <300 of δ–ALAD enzyme activity (high toxicity) have on average higher proteinuria (0.79) in contrast with those with 300–600 (low toxicity) with an average of 0.69, and those with higher activity of 600 (normal) with proteinuria of 0.46.

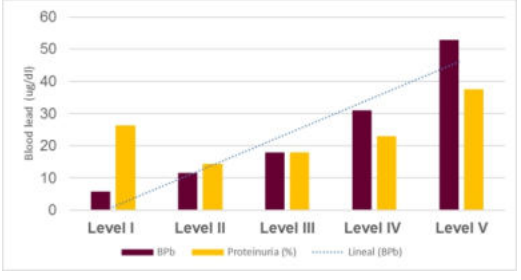

Figure 3. Correlation of Blood lead (BPb) and proteinuria in glass ceramic workers

Neuromuscular Conduction Velocity and Motor Nerve Coordination

Motor coordination and neuromuscular conduction velocity evaluated with an electronic device. Counting the number of hits (blows, strikes) that the patients was able to deliver on two metallic plates. Results indicate a reduction in coordination and neuromuscular conduction velocity (<18.4%) characterized by an average of 38.8 blows (hits)/10 sec, in contrast with 47.5 hits/10 sec of a population without exposure to Pb and with similar age characteristics, socioeconomic and cultural conditions, and who were clinically healthy.

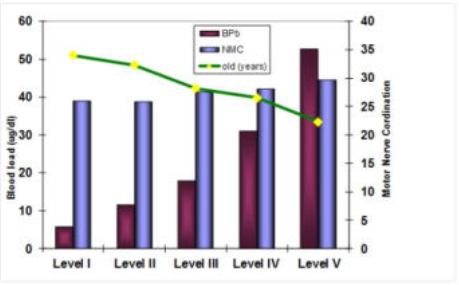

Figure 4. Correlation of Blood lead (Bpb), and neuromuscular conduction and motor nerve coordination.

Clinical Evaluation of Chronic Renal Damage

To discard contributing factors to chronic kidney damage independent of Pb exposure, we carried out a medical evaluation directed toward clinically defining the degree of Pb concentration, chronic kidney damage, and global evaluation of the patient. We reviewed 39 patients with positive tests for chronic kidney damage and high blood Pb concentrations. The clinical evaluation identified two patients with Type 2 Diabetes Mellitus (T2DM), one of whom with high blood pressure; these two patients presented factors that did not permit the association of intoxication with Pb with the possible related chronic kidney problems. In the remainder of patients we did not find pathological entities that could concur with the time of exposure to Pb; thus, these patients have, as most probable etiological factor BPb poisoning-associated chronic kidney damage. The latter additionally shows the efficiency of application of the screening and selection of the study group.

Clinical Evaluation of Lead Poisoning

The patients reviewed exhibited frank data of motor incoordination, neuromuscular coordination alterations, gastrointestinal and circulatory disorders, behavioral alterations, and conditioning of minor diseases due to the pathological process related with Pb poisoning. In the case of chronic kidney disease, we did not find signs of kidney insufficiency (kidney failure). However, we did find data of recurrent urinary infections and of manifestations of anomalous urinary excretion, which is in agreement with the findings of the general urine examination.

Worker Safety with Regard to Lead Poisoning

The medical evaluation also allows for detecting whether there is a great number of workers with total ignorance of the exposure, absorption, intoxication, risks, and forms of protection in the different aspects of occupational exposure to lead. Additionally, inadequate management detected on the part of the worker in terms of protection and safety measures and an absolute insensitivity to and unfamiliarity with the possibility of contaminating their relatives with lead, leading to occupational contamination in their households. These same workers exhibited indifference and even inattention to the safety and hygiene measures recommended in some companies, the large part of this due to the lack of information concerning then problem and the demonstration of insensitivity, thus preferring convenience and speed. It is important to emphasize that the protection and safety measures described by the worker are, in their majority, inadequate, deficient, and poorly applied. It is noteworthy that some companies that employ adequate protection systems or that certified as lead-free have contracts with workers with high concentrations of Pb in blood, possibly due to lead distribution phenomena. Thus, it is of great importance to determine the concentration of lead in blood prior to contracting the services of the worker, to avoid having labor problems deriving from exposures prior to the present employment event.

Epidemiological Considerations

In the sample of workers studied, we found 58% with a BPb concentration of >15 µg/dl, and in 12% of the workers, of >45 µg/dl. This sample considers solely 58% of the total of the population studied initially, due to the type of activity performed

by the workers that considered of lesser risk. The latter indicates that of the total population considered initially, 34% is found with BPb levels of >15 µg/dl and 7% had BPb concentrations of >45 µg/dl. If we were to engage in a simple extrapolation to a total population dedicated to glass ceramic work, we would have an estimate of 21,000 workers with BPb levels of >15 µg/dl and 4,900 workers with BPb concentrations of >45 µg/dl. In the case of chronic kidney damage, the same linear extrapolation would yield a total 11.9 % of workers with chronic kidney damage, which permits us to predict the presence of >8,310 cases of patients evolving with chronic kidney damage. Evidently, these estimates are linear and relatively lax; however, they indicate the magnitude of the problem that the Health Sector can confront in a brief period.

Conclusions

1. The sample of workers studied has a great dispersion in the distribution of age and employment seniority, which increased the dispersion in different variables dependent on Pb exposure.
2. There is overwhelming evidence of the presence of exposure, absorption, and intoxication with lead in the population of glass ceramic workers of Dolores Hidalgo, Guanajuato, Mexico.
3. A high percentage of the population presents problems that evolve into the generation of chronic kidney diseases, due to Pb poisoning.
4. There is evidence of concomitant diseases and physiopatho logical alterations induced by Pb poisoning.
5. There is a reduction in motor coordination, attention problems, behavioral alterations, and incidence alterations in the general status of the workers due to exposure to Pb.
6. Chronic exposure to Pb is such that redistribution factors could be presenting that render the toxic manifestations of Pb concentration in blood independent.
7. Chronic poisoning by Pb and chronic kidney damage is evolving in a population with very few outstanding and specific clinical manifestations, which renders impossible the clinical detection of the latter.
8. According to the epidemiological analysis, a great public-health problem could be incubating, if these patients evolve with chronic kidney damage or with chronic kidney failure.
9. Workers lack the information necessary for establishing protective measures for themselves and their families.
10. It is apparent that the companies' protection and safety measures are very deficient or, in some cases, inexistent.
11. Exposure to Pb is surely resulting in a reduction of worker productivity.

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