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Research Article

Arsenic and Lipid Balance in Workers Exposed to Urban Pollutants

Francesco Tomei[1*], Federica De Marco[1], Donato Pompeo De Cesare[1], Grazia Giammichele[1], Carmina Sacco[1], Gianfranco Tomei[2], Silvia Corsale[1], Roberto Massimi[1], Luciana Fidanza[1], Pasquale Ricci[3], Carlo Monti[4]

[1]Department of Anatomy, Studio Giolda s.r.l., Branch of Occupational Medicine via Monte delle Gioie, Rome, Italy;[2]Department of Human Neurosciences, Sapienza University of Rome, Piazzale Aldo Moro, Rome, Italy;[3]Department of Anatomy, Histology, Medical-Legal and the Orthopedics, Sapienza University of Rome, Rome, Italy;[4]Croce Rossa Italiana-Italian Red Cross

ABSTRACT

Background: Previous studies in the literature showed that exposure to low doses of arsenic can cause damage to various organs and tissues. The purpose of this study is to evaluate the possibility that arsenic can also cause alterations in the lipid structure of workers (drivers and road operators) professionally exposed to low doses of arsenic due to exposure to urban pollution.

Materials and methods: The study was conducted starting from an initial sample of 1500 Municipal Police workers in a large Italian city. The correlation indices (r) and multiple linear regression (β) between urinary arsenic and lipid profile (total cholesterol, High-Density Lipoprotein cholesterol, Low-Density Lipoprotein cholesterol and triglycerides) were calculated. Student's t-test and chi-square test between the various groups were also calculated to check for any differences.

Results: Pearson indices and multiple linear regression between urinary arsenic, total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides are not statistically significant; the only significant data that seem to influence total cholesterol is represented by age and job ($p<0.005$), while HDL cholesterol seem to be influenced by gender ($p<0.05$) The value of urinary arsenic, total cholesterol and LDL is higher in the group of road operators ($p<0.005$) compared to drivers.

Conclusion: The results obtained did not show a sure correlation between the levels of arsenic and the lipid profile and they lead us to believe that exposure to the very low levels of arsenic from urban pollution does not cause effects on the lipid profile and therefore these would be the need of new and original operating protocols, with the inclusion of innovative parameters relating to the presence of arsenic. The alteration of the lipid parameters detected could depend on the amount of dose absorbed, also by other pollutants according to a hermetic mechanism.

Keywords: Workers; Arsenic; Lipid structure; Urban pollution

INTRODUCTION

Arsenic is a semi-metal commonly found in nature [1]. The inorganic form is basically represented by arsenite (trivalent form) and arsenate (hexavalent form), both of these compounds are toxic to human health. Trivalent arsenic is considered the more toxic of the two [2]. Inorganic arsenic (As) is rapidly absorbed by the respiratory or gastrointestinal route (generally over 50% of the dose); The absorption percentage is lower by inhalation and very limited by dermal exposure [3,4]. This metalloid is extremely toxic to all animals. In mammals, inorganic arsenic, as well as its organic compounds, are

Correspondence to: Francesco Tomei, Department of Anatomy, Studio Giolda s.r.l., Branch of Occupational Medicine *via* Monte delle Gioie, Rome, Italy, E-mail: segreteria@spinoff-sipro.it

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converted into methylated metabolites, which are rapidly excreted. After digestive absorption, the inorganic As undergoes a process of methylation (monomethylated and methylated) at the liver level, it is transformed into compounds with less toxicity (monomethylarsonic and dimethylarsinic acid) and then excreted through the urine [5,6]. During the methylation process, the pentavalent inorganic as is transformed into tetravalent and into very reactive and toxic trivalent compounds. In humans, the metabolism of as is rapid. In case of intoxication more than half of the absorbed as is eliminated within forty-eight hours. Immediately after its absorption, it is found in the blood and the urine which for this reason are considered biological biomarkers of recent exposure; later it accumulates in the hair and nails which are therefore considered biomarkers of chronic exposure. In urine, inorganic as is present in a small percentage in trivalent and pentavalent form and as monomethylarsonic acid (this fraction of arsenic is greater in case of hepatic dysfunction), while a higher percentage is made up of dimethylarsonic acid. There are also complex arsenical compounds whose percentage varies according to the type of diet which are not metabolized but excreted unchanged [7].

Inorganic arsenic can pass the placenta and cause fetal damage, and various organs and systems are also considered toxic: Lungs, skin, kidneys and liver, especially in chronic intoxication [5].

The main cause of arsenic toxicity is its high presence in drinking water: It can get contaminated by pesticides, deposits of natural minerals or arsenic compounds not properly disposed [6]. Humans are also exposed to arsenic dispersed in air or food such as molluscs, crustaceans, poultry and fish [8,9]. It can also be found in urban pollution, where it exists mainly in the form of particles adsorbed with other metals such as suspended Atmospheric Particulate Matter (TSP). The form present in environmental pollution comes from natural sources (such as forest fires and volcanic eruptions) but also from industrial emissions (it is used in the processing of many metal alloys and glass) from the incineration of various types of waste including urban waste, medical waste, hazardous waste, as well as from coal-fired power plants, power plants, oil industries and foundries [10,11]. Annual global emissions from industrial and disposal sources are about three times as high as those from natural sources. Most studies of chronic arsenic exposure tend to focus on the description of cutaneous manifestations, however, other studies show that chronic exposures can also affect other organs and systems [12]. In the air, arsenic exists mainly adsorbed to atmospheric particulate; usually present as a mixture of arsenite and arsenate, and therefore, people working in these areas are potential arsenic receptors [13]. The present research follows previous studies in which the differences in exposure to arsenic were analyzed in the different types of work and tasks. The results obtained showed that exposure to as was higher in road operators compared to drivers and in outdoor workers in urban areas compared to outdoor workers in rural areas [5]. In other studies it was also observed that the exposure to As is responsible for a multisystem syndrome with involvement of the skin, of the hematopoietic and gastrointestinal system, it's also related to cardiovascular, neurological, diabetes, alopecia, hematological alterations and pulmonary fibrosis [14-17]. On the other hand, there are few studies in the literature that analyze low-dose lipid alterations. Experimental studies on rats have recently shown changes in some parameters of the lipid profile correlated to chronic exposure to arsenic [18-20].

The aim of this research is to analyze whether arsenic present in urban pollution can alter the lipid structure of professionally exposed workers.

In our previous research proposed the possibility that urban pollution can cause alterations in the lipid structure and we found that neither benzene nor cadmium, present in very low doses in urban air, cause alterations in the lipid structure [21,22].

MATERIALS AND METHODS

The study was conducted on an initial sample of 1500 outdoor Police workers of a big Italian city. We monitored their levels of urinary arsenic, total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides and all the other variables necessary for the study, as indicated below. The workers of group 2 were assigned to control vehicle traffic on roads and areas with high and medium density, at junctions, parking lots and limited traffic areas; they were not equipped with protective equipment against dust and fumes from traffic pollutions. The workers of group 1 were assigned to specific interventions in case of road accidents and other activities including driving a car as a driver or a "second on patrol"; their cars are equipped with air conditioning units and filters. Even motorcyclists were assigned to traffic control and specific interventions in case of road accidents and other activities, they are not equipped with protective device against dust and fumes coming from traffic. All these activities were performed by workers for at least 80% of the total work time (7 hours a day for at least 5 days a week). For inclusion in the study, each worker was administered a questionnaire, in the presence of a doctor, with a physiological history and past and recent medical history. The questionnaire also included questions in the binary system (yes/no), related to dyslipidemia, hypecolesterolemia and familial hypertriglyceridemia, cardiovascular disease, hypothyroidism collected. The pharmacological history was collected in order to verify the assumption of drugs for the treatment of diseases related to the lipid formation or that could interfere with it (antiretroviral drugs, anabolic agents, immunosuppressants, contraceptives, cortisone drugs and trans-retinoic acid). Voluptuous habits such as cigarette smoking (smokers and non-smokers), alcohol consumption and out-of-work activities in contact with possible sources of arsenic were evaluated. As to the smoking habitat we considered smokers, ex-smokers and non-smokers. According to the 2014 World Health Organization classification, the person who claims to have never smoked or smoked less than 100 cigarettes in his life and currently does not smoke is considered non-smoker; currently he has not smoked, for more than 6 months, the subject who claims to have smoked more than 100 cigarettes in his life and currently smokes every day or the person who currently does not smoke but stopped smoking less than 6 months before. They underwent a medical examination and a blood test to detect the following parameters: total cholesterol, HDL, LDL and triglycerides. The workers were

made comparable by age, seniority, cigarette smoking habits (number of cigarettes per day) (Table 1), alcohol habit (number of glasses per day) and body mass index (BMI) (kg/m2). Workers with less than 1 year of employment were excluded. The laboratory performed the dosage of total cholesterol, HDL, LDL and triglycerides, the normal levels of all the analyzed parameters are those normally used by the laboratory for clinical analysis: Total cholesterol<200 mg/dl, LDL cholesterol 70 mg/dl-180 mg/dl, HDL cholesterol 40 mg/dl-80 mg/dl and triglycerides 150 mg/dl-200 mg/dl.

	Total sample 122	Group 1 38	Group 2 84	P
Age (years) (Media ± DS) (Range)	53.77 ± 8.5781 (38-70)	51.73 ± 8.07961 (39-70)	54.690 ± 8.6845 (38-64)	0.0781
Light of service (years) (M ± SD) (Range)	14.295 ± 8.7251 (1-36)	12.13 ± 8.0796 (1-34)	15.012 ± 8.9759 (5-36)	0.1783
Sex (M/ F)	82/40	28/10	54/30	-
Habitude to smoke (%)	38/122 (31.14%)	13/38 (34.21%)	25/84 (29.76%)	-

Table 1: Characteristics of the examined sample.

Given that appreciable levels of arsenic are present in drinking water, we evaluated the residence of the workers in our study and included only workers who were living in the same city and who therefore drank water from the same aqueduct. To limit the intake of arsenic with the diet, considering the presence of metal in crustaceans, workers were strongly recommended not to eat this food for five days before the blood collection and urine sample collection.

Both traffic wardens and police drivers were considered having the same dietary habits and water supply throughout their working activity: All subjects worked in the same urban environment, were they being living for at least 5 years.

Urinary arsenic monitoring, expressed in µg/l (micrograms/liter), was performed for each subject at the end of their work shift. All workers were recommended to refrain from consuming food as meat offal, crustaceans and seafood and alcoholic beverages in the five days preceding the medical examination [22-24]. The blood collection and urine samples were collected and transported to the laboratory at +4°C, then stored at-20°C until analysis. The Jaffè method was used to determine urinary creatinine on all urine samples. After mineralization the acid urine samples were analyzed by atomic absorption with hydride generator (arsenic reduction to arsine). All urinary arsenic results were expressed in µg/l.

Each workers had given informed consent and all data were collected and processed anonymously. All participants agreed to take part in the screening program and were individually informed of their results. All data were collected and processed in accordance with the principles of the Helsinki Declaration. The mean and standard deviation of urinary arsenic were calculated, as well as the number of subjects with arsenic urinary above the limit value for the professionally exposed population, which, according to the latest guidelines of the ACGIH (2015) is 35 µg/l [25].

The Italian Society for Reference values suggests a Reference Value (RV) of urinary arsenic between 2.0 µg/l-15.0 µg/l in subjects non-occupationally exposed [26].

The doctors and lab technicians didn't know which samples came from the traffic wardens and police drivers, even though they both knew that a search was being made.

From the initial sample workers those with the following confounding factors were eliminated at the end from the study:

-Smoking habits: 44 workers

-BMI>30: 12 workers

-Drugs capable of interfering with lipid metabolism (contraceptives, cortisonics, trans-retinoic acid, antiretrovirals, anabolic agents, immunosuppressants): 20 workers

-History of dyslipidemia, hypecolesterolemia and familial hypertriglyceridemia, cardiovascular disease, hypothyroidism: 14 workers

-Alcohol consumption>0.5 liters/day: 6 workers

-Extra-work exposure (paints and fertilizers): 3 workers

This selection was aimed at eliminating the possible influence of these factors on any alterations of the urinary arsenic and/or the lipid profile of the sample under examination.

The resulting sample of 122 workers was further divided into 2 subgroup of the basis of the task:

- Class I: 38 workers with driving activities (28 males and 10 females).

- Class II: 84 road operators (54 males and 30 females).

Statistical analysis

The results for the urinary arsenic values and for those of the lipid parameters (total cholesterol, HDL, LDL, triglycerides) are expressed in terms of mean, Standard Deviation (SD) and range (min-max).

The comparison between the means was carried out using the T test, in the total sample and after subdivision on the basis of sex, BMI, seniority, chronological age and job.

The Pearson's correlation was calculated to verify the level of association between urinary arsenic values and lipid parameters with other factors that could be influencing (age, seniority, gender, BMI).

The multiple linear regression was performed, we considered the parameters of the lipid profile as dependent variable and urinary arsenic, sex, age, length of service and BMI as independent factors.

The results were considered significant when p-values were lower than 0.05.

RESULTS

The characteristics of the studied population as described above are shown in Table 1. None of the workers reported current or previous liver and kidney diseases, chemotherapy or use of drugs capable of interfering with the lipid metabolism (contraceptives, cortisone, trans-retinoic acid, antiretroviral, anabolic, immunosuppressants) in the last 6 months, a history of dyslipidemia, hypecolesterolemia and familial hypertriglyceridemia, cardiovascular disease, hypothyroidism, hobbies such as gardening or extra-work exposure to paints or fertilizers. None of the subjects reported eating food such as fish, crustaceans, rice, corn, mushrooms and poultry during the 4 days prior to the urine sampling. Both traffic policemen and police drivers were considered having the same dietary habits and water supply throughout their working activity. All subjects worked in the same urban environment, where they had been living for at least 5 years. All urinary creatinine values were within the reference range recommended by the WHO (0.3 g/l-3.0 g/l). No subject had urinary arsenic values higher than 35 µg/l proposed by ACGIH [24].

The values of urinary arsenic values were higher in the group 1 (19.048 ± 12.9102) than group 2 (7.5 ± 4.2795) and this result was statistically significant (p=0.0001). The total cholesterol values (p=0.0013) and LDL cholesterol (p=0.0030) were higher in group 1 than group 2 (Table 2).

	Total sample 122	Group 1 38	Group 2 84	P
Total cholesterol (M ± SD) (Range)	207.50 ± 41.338 (106-317)	188.28 ± 38,15955 (116-297)	215.45 ± 40.623 (106-317)	0.0013
Triglycerides (M ± SD) (Range)	99.96 ± 66.209 (20-416)	101.93 ± 68.994 (34-351)	97.75 ± 65.959 (20-416)	0.5
HDL cholesterol (M ± SD) (Range)	53.24 ± 12.622 (21-91)	52 ± 11.29 (32-74)	54.06 ± 13.161 (21-91)	0.2
LDL cholesterol (M ± SD) (Range)	131.12 ± 38.748 (9-228)	106.625 ± 36.36 (50-214)	138.04 ± 37.458 (9-228)	0.0030
Arsenic urinary (M ± DS) (Range)	15.43 ± 12.196 (3-34) micrograms /liter	7.5 ± 4.2795 (3-21)	19.048 ± 12.9102 (10-34)	0.0001

Table 2: Lipid balance in the two groups.

In group 1, 71.42% of traffic policemen (60 workers) have urinary arsenic values higher than 15.0 µg/l proposed by SIVR, in group 2 10.52% (4 workers) [25]. This difference is statistically significant (p<0.05, chi square test). All workers had urinary arsenic values<35 µg/l proposed by ACGIH [24].

No statistically significant correlation and regression (p two-tailed<0.05) was found between urinary arsenic, total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides. The multiple linear regression (p<0.05) seems to point out that the total cholesterol is influenced by age (p=0.011) and by the task (p=0.017), while HDL cholesterol by sex (p=0.033).

In conclusion we did not find a, no statistically significant correlation between urinary arsenic, total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides.

It appears from the multiple linear regression that total cholesterol is influenced by age and job title, while HDL cholesterol is influenced by gender.

DISCUSSION

The organic arsenical compounds are generally considered not very absorbable and their absorption is related to their water solubility. They are also easily eliminated with feces and urine; in fact they are subject to detoxifying hepatic bio methylation, therefore the organic arsenicals are less toxic and more easily excreted [4,5].

The environmental exposure to arsenic can occur near foundries and anthropic settlements for the production of energy (coal-fired power plants) and oil industries. The exposure can also occur by skin contact with contaminated soil and less frequently with arsenic-containing pesticides. The International Agency for Research on Cancer and the U.S. EPA, basing on the evidence in humans, classified the inorganic as a carcinogen and included it respectively in group I and in group A [27,28]. The mechanism of Carcinogenesis is not well known, but there is evidence that the exposure can generate free radicals and other reactive species in biological systems. The possible mechanisms include genotoxicity, oxidative stress, and inhibition of DNA repair, promotion of tumorigenesis, co-carcinogenesis, cell proliferation but also alterations in signal transduction or DNA methylation. More mechanisms can interact with each other [7].

Arsenic in humans can cause a number of diseases that include skin lesions (hyperpigmentation, melanosis, keratosis), respiratory problems (chronic cough, shortness of breath, bronchitis), effects on the nervous system (neuropathies, neurobehavioral disorders, loss of memory, low IQ, attention disorder), cancer in numerous organs (skin, lung, bladder) and effects on the reproductive system (complications during pregnancy, fetal anomalies, premature birth, low birth weight), as well as cardiovascular diseases and diabetes [3,29].

Studies on substances dispersed in urban pollution deriving from combustion processes can show the correlation between these substances and oxidative damage to DNA and an increase in blood lipids following the action on insulin resistance and lipid peroxidation with the result of a metabolism moved on lipogenesis and suggest the possible existence of a relationship between atmospheric pollution and altered lipid metabolism with increases in the value of LDL cholesterol in serum [30-33]. The possible mechanisms of action were described in the literature to explain the alterations induced by the various components of urban pollution: The release in the circulatory stream of pro-oxidative and pro-inflammatory mediators able to alter the LDL cholesterol already present in the blood, the direct action on the heart and blood vessels of ultrafine particles translocated in the systemic circulation which would lead to a greater accumulation of LDL cholesterol in the vessels [34-36]. We can hypothesize that the various substances dispersed in urban pollution, including arsenic, could act on the lipid peroxidation and that they may play a synergistic role on lipid metabolism together with the other chemical pollutants present in the atmosphere [37-40]. The data of our study suggest that arsenic, present in urban pollution, is responsible for cardiovascular alterations, vasculotoxic and carcinogenic effects, responsible for alterations in lipid metabolism [41-45].

CONCLUSION

Our study induce to believe that also the general population could be exposed to higher values of urban pollution than acceptable limits and could be affected by the negative effects on the lipid structure. Although it remains data to confirm, surely the importance of monitoring exposed workers is supported by higher value of urinary arsenic and total cholesterol, HDL cholesterol and LDL cholesterol in traffic policemen than drivers. The correlation was not statistically significant and regression (two-sided $p<0.05$) between urinary arsenic, total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides, it was significant that 64 workers (road workers and drivers) out of 122 have urinary values of arsenic higher than 15.0 μg/l, limit proposed by SIVR for the general population. The results obtained did not show a certain correlation between the levels of arsenic and the lipid profile and would lead us to believe that exposure to the very low levels of arsenic from urban pollution does not cause effects on the lipid profile and therefore the need to new and original operating protocols, with the inclusion of innovative parameters relating to the presence of arsenic. The alteration of the lipid parameters detected could depend on the amount of dose absorbed, also by other pollutants according to a hormetic mechanism.

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