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RESEARCH FOR THE EFFECTS OF CRONIC INORGANIC ARSENIC INTOXICATION ON CERTAIN BIOCHEMICAL AND PHYSIOLOGICAL PARAMETERS

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ABSTRACT

In this study, it was aimed to research the changes in some biochemical parameters and blood pressure values of those exposed to inorganic arsenic by drinking water involving high level of arsenic for a long time. Forming two groups- the control group and the one composed of those exposed to chronic arsenic, the values were compared between the groups. By taking venous blood samples from the subjects, blood glucose, triglyceride and total cholesterol levels were determined in their serums. Also, by taking their blood pressure, their diastolic and systolic blood pressure values were determined. It was found that those exposed to chronic arsenic had higher blood glucose, triglyceride, total cholesterol levels and blood pressure values than the control group. The mean values of those exposed to chronic arsenic and the control group were as follows respectively: blood glucose levels 139.90 ± 36.22 mg/dl vs 96.86 ± 21.90 mg/dl, triglyceride levels 189.28 ± 43.76 mg/dl vs 131.33 ± 35.14 mg/dl, total cholesterol levels 156.34 ± 29,61 mg/dl vs 118.53 ± 46.15 mg/dl, diastolic blood pressure 81.92 ± 10.59 mm Hg vs 71.50 ± 7.27 mm Hg, and systolic blood pressure 138.46 ± 21.59 mm Hg vs 114.50 ± 13.07 mm Hg. As a result of statistical analysis, the values were determined to be significant ($p<0.001$).

Consequently, it can be said that a long term exposure to high amount of inorganic arsenic in drinking water have adverse effects on the biochemical parameters in humans and that the risk of different ailments in these subjects may increase depending on the oxidative stress caused by arsenic.

Key Words: *Arsenic, Intoxication, Biochemical parameters, Blood pressure*

İNSANDAKİ KRONİK İNORGANİK ARSENİK İNTOKSİKASYONUNUN BAZI BİYOKİMYASAL VE FİZYOLOJİK PARAMETRELERE ETKİLERİNİN ARAŞTIRILMASI

ÖZET

Bu çalışmada uzun süre yüksek oranda arsenikli içme suyu ile inorganik arseniğe maruz kalan kişilerde bazı biyokimyasal parametre ve kan basınç değerlerinde meydana gelen değişimlerin araştırılması amaçlandı. Çalışmada kronik arseniğe maruz kalan kişiler ve kontrol grubu olmak üzere iki grup oluşturularak değerler gruplar arası kıyaslandı. Çalışmaya katılan kişilerden venöz kan alınarak, serumlarında kan glukozu, trigliserit ve total kolesterol seviyeleri belirlendi. Ayrıca bu kişilerin tansiyonu ölçülerek diastolik ve sistolik kan basınç değerleri tespit edildi. Kronik arseniğe maruz kalanlarda kontrol grubuna göre kan glukozu, trigliserit ve total kolesterol seviyeleri ile kan basınç değerlerinin yüksek olduğu tespit edildi. Kronik olarak arseniğe maruz kalan kişiler ile kontrol grubu değerleri ortalamaları sırasıyla kan glukoz düzeyleri 139,90 ± 36,22 mg/dl vs 96,86 ± 21,90 mg/dl, trigliserit düzeyleri 189,28 ± 43,76 mg/dl vs 131,33 ± 35,14 mg/dl, total kolestrol düzeyleri 156,34 ± 29,61 mg/dl vs 118,53 ± 46,15 mg/dl, diastolik kan basıncı 81,92 ± 10,59 mm Hg vs 71,50 ± 7,27 mm Hg, sistolik kan basıncı 138,46 ± 21,59 mm Hg vs 114,50 ± 13,07 mm Hg olarak tespit edildi. Yapılan istatistiksel analiz sonucunda değerlerin anlamlı ($p<0,001$) olduğu tespit edildi.

Sonuç olarak uzun süre içme suyundaki yüksek orandaki inorganik arseniğin insanlarda biyokimyasal parametreleri olumsuz yönde etkilediği ve arseniğin oluşturduğu oksidatif strese bağlı olarak bu kişilerde farklı hastalıkların oluşma riskini arttırabileceğini söyleyebiliriz.

Anahtar kelimeler: *Arsenik, İntoksikasyon, Biyokimyasal parametreler, Kan basıncı*

1. INDRODUCTION

Arsenic is the top list toxic substance known in drinking water [1]. Arsenic in drinking water is defined as carcinogenic substance by World Health Organization (WHO) [2]. International Agency for Research on Cancer (IARC) shows arsenic in the chemical class (Group 1) whose cancer causing feature has been proved [3].
Arsenic is also a trace element for human body; that is, it is required for the body in only a minute amounts. For the general population, daily almost 0.200 mg/kg arsenic intake is required [4]. However, high levels of intake have negative effects on health [5].

Arsenic intake can be in three ways: by breathing, food and water consumption and dermal adsorption. Although arsenic intake is through drinking water, food and breathing, the most crucial exposure is through drinking water. Arsenic is colourless, odourless and flavourless, so it can't be traced in drinking water through sense organs; lab tests are required for analysis. Inorganic arsenic is more toxic than organic for human body because organic arsenic can be discharged easily by the body in normal conditions [6, 7].

After arsenic intake, it is stored first in liver, lungs, kidneys and heart. A very small amount also accumulates in muscles and nerve tissues. Within 2-4 weeks after arsenic intake, it starts to accumulate in nails, hair and skin by being bound by keratin sulfhydryl groups [8].

Because arsenic and arsenic compounds are carcinogenic in humans, contamination of drinking water with arsenic is an important public health problem. Inhaling inorganic arsenic might lead to lung cancer, while inorganic arsenic intake through food might cause skin, bladder, kidney, colon, liver and lung cancer. After arsenic intake, many different organs like skin, respiration system, cardiovascular system, immune system, genital and urinary system, digestive system and neural system can be affected [6]. Among the overall negative effects of exposure to arsenic are cardiovascular and peripheral vascular diseases, vascular diseases (Black foot), gangrene, development anomalies, neurologic and behavioural disorders, diabetes, hearing loss, portal fibrosis, hematologic disorders (anaemia, leukopenia and eozinophilia), bronchitis, various skin lesions, hypertension, oedema, ulcer, miscarriage, stillbirth, premature birth, malaise, weight loss, hypokinesia and damage in immune system [9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24].

The main symptoms of chronic effect of long term exposure to arsenic through food, drinking water and drugs are diarrhoea or constipation, rash on skin, pigmentation hyperkeratosis and arsenicosis [5, 7, 12]
World Health Organization, depending on its studies, decreased the arsenic amount in drinking water from 50 μ/L to 10 μ/L in 1993 and declared the water with arsenic concentration above 10 μ/L as toxic [2]. The max limit value of arsenic in drinking and utility water permitted in Turkey was 50 μg/L until February 2005. From that date on, the max limit value was decreased to 10 μg/L by the Regulation on Drinking and Utility Water and a 3-year transition period was proposed. Accordingly, the limit value for drinking and utility water has been 10 μg/L since February 2008 [25].

In a study, it was found that being exposed to less than 50 ppb arsenic through drinking water during pregnancy might cause low birth weight. It has also been proved that chronic arsenic intake through drinking water cause micronucleus formation in peripheral blood lymphocytes, mouth mucosa and urinary tract cells indicating carcinogen effect. It has also been found that health problems arising from arsenic aggravate with malnutrition and that arsenic and smoking are effective synergically in lung cancer occurrence. In a study conducted on townspeople who had used drinking water with high arsenic content (average 412 ppb), it was determined that there were significant differences in replication index in lymphocytes and there was decrease in proliferation ability [26]. In a study on 891 adults in South Taiwan in 1988, it was found that diabetes mellitus prevalence increased depending on arsenic intake. In another study, it was shown that there was a relation between type–2 diabetes and drinking water of 700-930 μg/L arsenic level [27]. In a study on 382 male and 516 female subjects in Japan analysing the effect of long term inorganic arsenic intake on cardiovascular system, hypertension prevalence was reported to increase 1.5 times. In the USA, mortality rate due to vascular diseases depending on arsenic in drinking water of 30 states was researched and standard mortality rates due to artery, arteriole and capillary diseases (SMR) were found to be 1.9 in females and 1.6 in males. It was found that mortality risk from

liver, lung and urinary bladder cancer arising from lifelong drinking of 1 litre of drinking water involving 50 ppb arsenic was 13 in 1000 [10, 28].
Samples taken from 40 different drinking water sources in and around Emet town of the city of Kütahya showed that their arsenic content ranged from 0 to 10.7 mg/L. The village with the highest arsenic dose also suffered from the most arsenic poisoning cases (30.9%). In İğdeköy, where the arsenic concentration in the water reached to 8.9-9.3 mg/L, 30 cases were observed hinting arsenic poisoning [29]. In another study in İğdeköy, hair and blood samples were taken and comet assay and sister chromatid exchange (SCE), which is a bio indicator of genotoxic damage, were analyzed. Comet scores were found to be high in those exposed to arsenic, but comparing their SCE results with the control group, no significance was found. While max arsenic concentration determined by WHO is 0.01 mg/l in drinking water, 0.01–1 mg/kg in hair and 2–23µg/lt in blood, the values in the samples were 1.70mg/l, 89 (39–169)mg/kg and 115 (114–264)ug/l respectively. Consequently, it was determined that arsenic exposure cause serious DNA damage and the mutagenic effect provide a basis for cancer [30].

2. MATERIAL & METHOD

After preliminary surveys, the area was chosen İğdeköy village of Emet town of Kütahya in terms of chronic arsenic exposure. Recent researches have shown that chronic arsenic intoxication in the area is very high (according to the analysis conducted by Ministry of Environment and Forestry the arsenic concentration in the well water in İğdeköy was 1.133mg/L in 2001, while it was 8.9-9.3 mg/L in 2005).

In our study, the study group was composed of 26 villagers of İğdeköyü between the ages of 22 and 57 with age average 39.15 (15 females, 11males). The control group was composed of 20 volunteers with an average age of 37.55: 10 males and 10 females with no systematic illnesses who don't drink or smoke and haven't used any medicine for the last month.

Both the control and the study group had systolic and diastolic blood pressure checked from their right arms after a 15 min rest.

Biochemical analysis

5 mL venous blood samples were taken from the participants into vacoteiner tubes after at least 12 hr hunger. Blood samples were immediately centrifuged and then their serum parts were separated and put into different eppendorf tubes to be kept in deep freeze at – 20 ^{o}C until they were to be studied. Later, these serums were studied on with auto analyzer for blood glucose, total cholesterol and triglyceride parameters.

Statistical analysis

The data were recorded on "SPSS for Windows 15.0" statistical package program for statistical comparisons using Mann-Whitney U test. The significance value of $p<0.001$ was accepted. Mean values and standard deviations (SD) were found according to groups.

3. FINDINGS

Both groups' systolic and diastolic blood pressures were determined using biochemical tests. Comparing the results, an increase was observed in the values of those exposed to arsenic that. The mean and standard deviation of the results in both groups were computed and statistical analysis between groups was conducted.
It was determined that blood glucose, total cholesterol and triglyceride levels and blood pressure values of those exposed to arsenic were higher than the control group. Table 1 shows the mean and standard deviation of biochemical parameters and blood pressure values.

	Arsenic intoxication group (n = 27) Srt. ± Std. Deviation	Control group (n = 20) Srt. ± Std. Deviation
Age	39.15 ± 9.31	37,55 ± 8.36
Blood Glucose (mg/dl)***	139.90 ± 36.22	96.86 ± 21.90
Triglyceride (mg/dl)***	189.28 ± 43.76	131.33 ± 35.14
Total Cholesterol (mg/dl)***	156.34 ± 29.61	118.53 ± 46.15
Diastolic Blood Pressure (mmHg)***	81.92 ± 10.59	71.50 ± 7.27
Systolic Blood Pressure (mmHg) ***	138.46 ± 21.59	114.50 ± 13.07

Table 1. Comparison of the values between the groups

***: p<0.001

In the arsenic intoxication group, the mean blood glucose level was found to be 139.90 ± 36.22 mg/dl and the mean triglyceride level was 189.28 ± 43.76 mg/dl, while the mean total cholesterol level was 156.34 ± 29.61 mg/dl. The mean diastolic blood pressure was 81.92 ± 10.59 mm Hg, while the mean systolic blood pressure was 138.46 ± 21.59 mm Hg.

In the control group, the mean blood glucose level was found to be 96.86 ± 21.90 mg/dl and the mean triglyceride level was 131.33 ± 35.14 mg/dl, while the mean total cholesterol level was 118.53 ± 46.15 mg/dl. The mean diastolic blood pressure was 71.50 mm Hg, while the mean systolic blood pressure was 114.50 mm Hg.

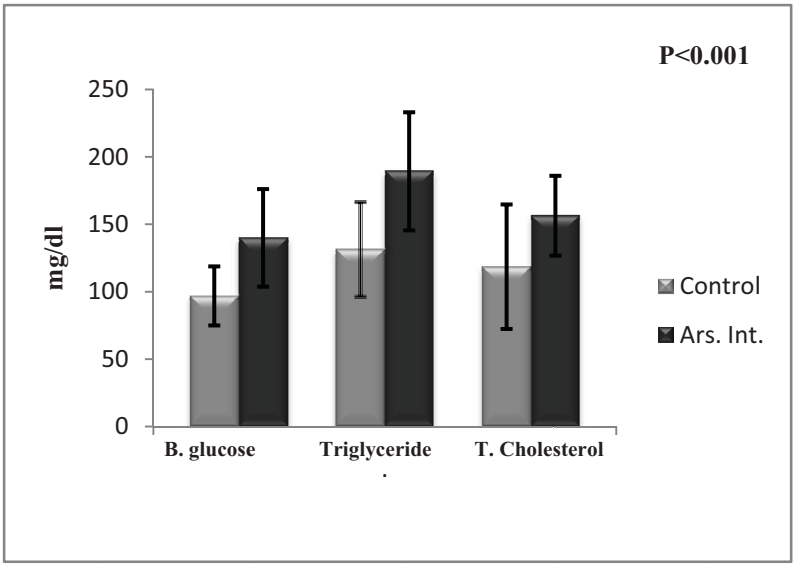

Figure 1. Comparison of the biochemical values between the groups

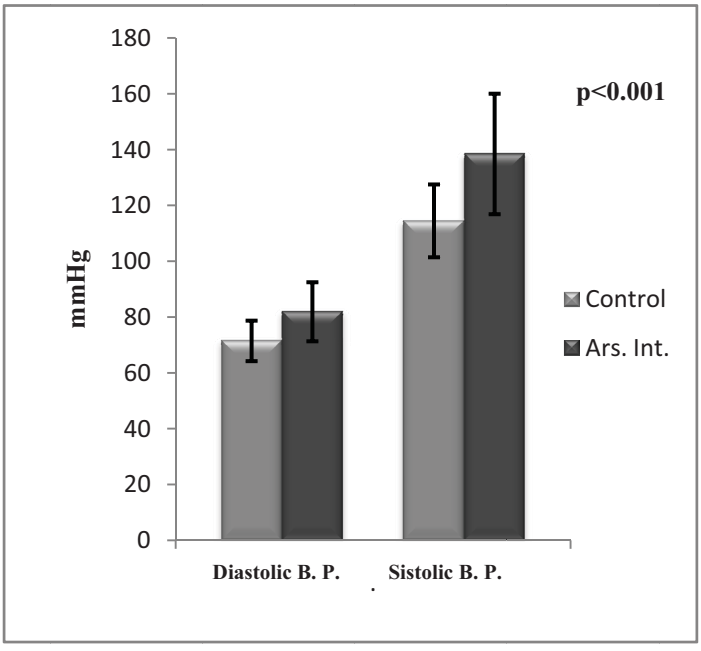

Figure 2. Comparison of the blood pressure values between the groups

Compared to the control group, it was found that in the arsenic intoxication group that there was 44.4% increase in blood glucose level, 44.1% increase in triglyceride level, 31.9% increase in total cholesterol level, 14.6% increase in diastolic blood pressure and 20.9% increase in systolic blood pressure. Statistical analysis showed that the increase in all the values was statistically significant ($p<0.001$).

4. DISCUSSION

Many health problems arise in those consuming drinking water with high inorganic arsenic concentration such as skin, bladder, lung, liver, kidney and prostate cancer. Furthermore, several studies determined that consuming drinking water with high inorganic arsenic concentration also provide a basis for many diseases as well as having a carcinogen effect.

In our study, certain biochemical parameters (blood glucose, triglyceride, total cholesterol) and blood pressure values of those drinking water contaminated with arsenic for a long time were compared to those of the control group. It was determined that those exposed to arsenic had higher values. Previous studies had shown that arsenic effected diabetes, hypertension, hyperlipidemia occurrence.

In our study, it was observed that blood pressure level in those exposed to arsenic was 44.4% higher than the control group, which was determined to be significant ($p<0.001$) as a result of statistical evaluation. J.A. Izquierdo-Vega et al. determined hyperglycemia, hyperinsulinemia and low insulin sensitivity in rats exposed to inorganic arsenic. It was determined that accumulation of reactive oxygen species (ROS) of hyperglycemia developing when exposed to arsenic leads to cytotoxic effects due to membrane phospholipid peroxydation, loss of membrane porosity and membrane intactness. They stated that ROS leads to protein changes and loss of protein effects [31]. U. Biswas et al. observed significant increase in the blood glucose levels of the goats exposed to arsenic after 6^{th} week [32]. Tseng et al. determined a correlation between arsenic intoxication and insulin independent diabetes [33]. Tsai et al. revealed a potential relation of drinking water with and chronic arsenic exposure mortality due to diabetes [34]. Rahman et al. conducted a study on copper plant and glassware workers and stated that there is a significant relation between arsenic exposure due to profession and diabetes [35, 36]. In our study, an increase was observed in the blood glucose levels of those exposed to inorganic arsenic chronically through drinking water. It was projected that the reason for this increase was insulin resistance

depending on oxidative stress arsenic caused in pancreas tissues and decrease in insulin sensitivity depending on oxidative damage arsenic caused in membrane proteins.

It was determined in our study that triglyceride and total cholesterol levels in those exposed to arsenic were 44.1% and 31.9% higher respectively than the control group. Wang et al., in their study in Taiwan, determined higher triglyceride and CHO/HDL rates in those exposed to arsenic compared to the control group. They stated that depending on the level of arsenic exposure, an increase would be observed in hypertension, hypercholesterolemia and abnormal LDH levels. In our study, it was observed that triglyceride and total cholesterol levels were significantly higher in those exposed to arsenic, which shows that a long term high level of arsenic intoxication significantly increase the hyperlipidemia, hypercholesterolemia and cardiovascular disease risks [37].

In our study, it was determined in the blood pressure levels that diastolic pressure was 14,6% higher and systolic pressure was 20.9% higher in those exposed to inorganic arsenic for a long time compared to the control group. In their study on rats, J.A. Izquierdo-Vega et al. found that the metabolic syndrome having a crucial role in insulin resistance caused by inorganic arsenic also effects hypertension and degenerative arteriosclerosis development process [31]. When superoxide radical of ROS formed by arsenic in tissues meet NO formed by endothelium cell, they turn into nonradical shape by sharing their unpaired electrons. As a result, the superoxide radical antagonize the vasodilatation effect of NO. It is argued that superoxide overproduced in the vein may be one of the causes of hypertension [38].

Consequently, we determined that a long term exposure to high level of inorganic arsenic in drinking water had adverse effects on the chemical parameters in people. We also found that higher values in those exposed to arsenic than the control group were statistically significant ($p<0.001$). We can say that metabolic syndromes depending on oxidative stress caused by arsenic in body tissues might lead to many illnesses. We can also say that especially due to the increase in the blood glucose level, insulin resistance occurred in these people and that due to insufficient insulin sensitivity, risk of diabetes increased. Arsenic is an important factor in increasing the risk of hypercholesterolemia, hypertension and cardiovascular disease not only due to the metabolic syndrome caused by diabetes but also due to the oxidative damage caused by oxidative stress.

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