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ASSESSMENT OF ARSENIC EXPOSURE FROM DRINKING WATER WITHIN A POPULATION GROUP IN COVASNA COUNTY, ROMANIA

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ABSTRACT. Numerous studies have shown that groundwater is naturally contaminated with arsenic exceeding 10 µg/l in the western and central area of Romania. Arsenic contaminated drinking water is a health hazard; therefore, the purpose of this study was to evaluate the exposure to arsenic in drinking water within a population group. In 2014 we recruited 25 subjects from Covasna County, Romania. Participants completed a questionnaire and we collected water samples from drinking water sources (springs and tap) and nail samples. Arsenic concentrations were determined by hydride generation atomic absorption spectrometry. Exposure doses and cancer risk were calculated individually for each subject, following a methodology developed by the US Agency for Toxic Substances and Disease Registry. Arsenic concentrations ranged from 0.5 to 91.8 µg/l, with mean 22.16±37.44 µg/l (mean±SD), in drinking water; and ranged from 0.04 to 100.30 µg/g, with mean 16.90±20.97 µg/g (mean±SD) in nail samples. Exposure doses were above MRL (minimal risk level) for chronic exposure for 3 subjects. Risk estimations predicted a theoretical risk of 5 excess cancer cases in a population of 10,000. Groundwater sources are a potential health hazard for the population in the area, thus due to the limitations of the present study, further studies are needed with extended no of participants and additional individual data.

Key words: *arsenic, drinking water, exposure assessment, cancer risk estimation, Romania.*

INTRODUCTION

Several studies have shown that in some regions of Romania the groundwater is naturally contaminated with arsenic (As). In a pilot study conducted in Arad County, Gelmann et al. (2013) measured inorganic arsenic (iAs) levels in drinking water of 54.4 ± 27.0 µg/l (mean ± SD). Kunrath et al. (2013) reported average iAs concentrations in water of 40.2 ± 30.4 µg/l (mean ± DS) in Arad County. Within the Arsenic Health Risk Assessment and Molecular Epidemiology (ASHRAM) study arsenic levels in drinking water were measured between 0.1 and 196 µg/l in Arad County, respectively, between 0.1 and 58 µg/l in Bihor County (Hough et al., 2010; Leonardi et al., 2012). Lindberg et al. (2006) measured the levels of arsenic in drinking water from two counties in Romania: median of 0.48 µg/dm^3 and a maximum of 24 µg/dm^3 in Bihor County, respectively a median of 0.70 µg/dm^3 and a maximum of 95 µg/dm^3 in Arad County. Another study conducted in Bihor and Arad counties reported arsenic levels in drinking water between 0 and 176 µg /l (Gurzau and Gurzau, 2001). In a study by Aposhian et al. (2000) water samples were taken from wells in Arad County, from which the study subjects consumed water. The arsenic concentrations measured in the water samples were between 2.8 and 161 µg/l. In a study conducted in Timis County, Romania, Bloom et al. (2014) measured drinking water arsenic concentrations ranging from 0.0 to 175.1 µg/l, with median 0.4 µg/l and 90th%tile 9.4 µg/l. Neamtiu et al. (2015) reported inorganic arsenic concentrations measured in drinking water from sources in Timis County between <0.5 µg/l and 175 µg/l, with an average of 8.6 µg/l and a median of 3.0 µg/l. Tudorache et al. (2011) measured arsenic concentrations in natural mineral water wells as high as 1505 µg/l, in a sampling point in Covasna, Romania and in the central area of Romania the authors found seven mineral water wells containing arsenic at concentrations of ten to a hundred times higher than the allowed limit of 10 µg/l. These wells were prohibited for human and animal use (Tudorache et al., 2011).

The data published in the scientific literature regarding arsenic contamination of groundwater in Romania shows that the population in those areas is exposed to arsenic levels higher than the allowed limit of 10 µg/l, recommended by the World Health Organization (WHO, 2017).

The purpose of this study was to assess the exposure to arsenic from water in a population group in Covasna County, Romania, by identifying the

sources of exposure to arsenic of the study population, analyzing arsenic levels in groundwater sources from Covasna city and in nail samples collected from the study subjects, by calculating arsenic exposure doses and estimating cancer risks due to exposure to arsenic in drinking water.

MATERIAL AND METHODS

Study population

In 2014 we recruited 25 subjects from the patients of the Cardiovascular Recovery Hospital „Dr Benedek Geza" from Covasna, Covasna County, Romania. The selection criteria were the following: age between 25 and 80 years; non-smokers or non-smokers in the last 2-3 years; stable housing in Covasna area for the last 10 years; more than 10 sessions of spa treatment at the Cardiovascular Recovery Hospital „Dr. Benedek Geza" Covasna; patients with ischemic heart disease, hypertension and/or arteriopathy; people with diabetes were excluded. The participants were identified by the doctor responsible for the spa treatment. Persons who met the selection criteria listed above were informed about the study objectives and were invited to participate in the study. Those who expressed a desire to participate in this study were offered to sign an informed consent form. Only the persons who signed the informed consent forms were included in the study.

Data on human exposure to environmental pollutants were collected using a questionnaire. Subjects were asked about housing, sources of pollution in the housing area, drinking water consumption, lifestyle, hobbies, habits/ behaviors (eg smoking), work history and exposure, and health status.

Drinking water sampling and analysis

Using the questionnaire data, the drinking water sources of the participants were identified. Water samples were collected from 6 mineral springwater sources in Covasna city, a sample from the city's water network and a sample from the water used in the spa treatment of patients. The water samples were collected in 50 ml srew-top decontaminated polyethylene containers, which were previously washed with water and detergent, rinsed

with distilled water and preserved with concentrated analytical grade nitric acid. The samples were labeled with a unique sample identification number and were stored on ice until transfer to the laboratory.

Water samples were analyzed for arsenic concentrations using a Zeenit 700 atomic absorption spectrometer with hydride generation system (Analytic Jena, Germany). The method is based on atomic absorption spectrometric measurement of the arsenic ion content of the sample, generated by the thermal decomposition of arsenic hydride. By this method, only arsenic III (As(III)) can be quantitatively determined, in order to avoid the errors of determination the other oxidation states must be transformed into As(III) before the determination, in order to be able to be transformed into hydride. As(III) is converted to hydride by reaction with sodium tetraborohydride in hydrochloric acid medium. The detection limit of the method was 0.5 µg/l. For digestion 25 ml of the sample was placed in the MARS 5 microwave digester vessel, 4 ml of nitric acid and 12 ml of hydrochloric acid were added, and left for 10 minutes in the microwave digester vessel, stirring occasionally. After the hermetic closure of the vessels, their digestion was started, lasting 20 minutes. After removing the vessels from the oven, they were allowed to cool to room temperature and ventilated to eliminate overpressure. The sample was diluted to 50 ml taking into account the dilutions in the final calculation.

The reduction of arsenic V to arsenic III was achieved by adding 10 ml of concentrated hydrochloric acid and 2 ml of potassium iodide-ascorbic acid to 25 ml of digested sample. It was heated at 50°C for 15 minutes. After cooling, it was brought to level with ultrapure water in 50 ml graduated flasks. In parallel, a control sample was performed using distilled water instead of the sample to be analyzed. The calibration curve was plotted using a standard solution, measuring the absorbance at different concentrations. After the calibration curve was drawn, the samples prepared were atomized in the quartz cell and the absorbance was measured with the Zeenit 700P atomic absorption spectrophotometer. The arsenic concentration, expressed in µg/l, was read directly from the calibration curve taking into account the dilutions made.

Nail sampling and analysis

Nail samples were collected from every subject with disposable metal nail clippers, disinfected with sanitary alcohol, in a quantity of at least 1 g,

from the toes. The nail sample was put into a ziplock plastic bag and labeled with a unique sample identification number. The transportation and storage of nail samples did not require special conditions.

The nail samples were analyzed for arsenic concentrations using a Zeenit 700 atomic absorption spectrometer with hydride generation system (Analytic Jena, Germany). The method is based on atomic absorption spectrometric measurement of the arsenic ion content of the sample, generated by the thermal decomposition of arsenic hydride. By this method, only As(III) can be quantitatively determined, so to avoid the errors of determination, the other oxidation states must be transformed into As(III) before the determination, in order to be able to be transformed into hydride. As(III) is converted to hydride by reaction with sodium tetraborohydride in hydrochloric acid medium.

Nail samples were pretreated; any visible dirt was manually removed, after which the samples were washed five times with ultrapure water, then soaked in acetone for 30 minutes and washed again five times with ultrapure water. Samples were kept in labeled vials, dried in the oven overnight at 50-60°C and dried for 2 hours. The dried samples were weighed and transferred into digestion containers with 5 ml of high purity nitric acid. The digestion process took place in a MARS 5 microwave digestion system, for 20 minutes. After removing the vessels from the oven, they were allowed to cool to room temperature and ventilated to eliminate overpressure. After cooling, each sample was transferred to a 15 ml flask and diluted to 15 ml with ultrapure water.

The calibration curve was plotted using a standard solution, measuring the absorbance at different concentrations. After the calibration curve was drawn, the samples prepared were atomized in the quartz cell and the absorbance was measured with a Zeenit 700P atomic absorption spectrophotometer. The arsenic concentration, expressed in µg/l, was read directly from the calibration curve taking into account the dilutions made. The method detection limit obtained was 0.5 µg/l.

Data analysis

Descriptive statistical analysis of the questionnaire data was performed with MS®Excel.

Exposure dose calculation

Arsenic exposure doses via drinking water ingestion were calculated using Exposure Dose Calculator, belonging to the US Agency for Toxic Substances and Disease Registry (ATSDR) of the CDC (Center for Disease Control and Prevention).

Exposure doses from ingestion of water were calculated using the following equation (ATSDR, 2005): ED = (C x IR x EF) / BW; where, ED = exposure dose [mg/kg /day]; C = concentration of contaminant in water [µg/l]; IR = intake rate of water [l/day]; EF = exposure factor (unitless); BW = body weight [kg].

Exposure doses were calculated individually for each study participant taking into account: the source from which the participant drinks water and the arsenic concentration measured in the water sample collected from the respective source, expressed in µg/l; the amount of water consumed daily by each participant, expressed in l/day; and the body weight of the participant, expressed in kg.

The exposure dose, expressed in milligrams per kilogram body weight per day (mg/kg/day), is an estimate of the amount of a substance a person comes in contact with, as a result of its activities and habits. Estimating an exposure dose involves determining how much, how often and for how long a person or population may come in contact with a particular chemical, at a certain concentration within a specific environmental factor (ATSDR, 2005). Exposure factor takes into account frequency, duration and exposure time (ATSDR, 2005). Body weight is used in the exposure dose calculation equation to express doses that can be compared within a population. When exposed to the same amount of a substance, people with a lower body weight will receive a relatively higher dose of that substance compared to people with a higher body weight (ATSDR, 2005).

Cancer risk estimation

The risk of cancer from exposure to arsenic in water was estimated according to the ATSDR (Agency for Toxic Substances & Disease Registry) public health assessment guidance manual, using the Exposure Dose Calculator (ATSDR, 2005). According to the quantitative risk assessment

methodology, the exposure doses calculated for the measured concentrations are multiplied by an oral slope factor, calculated by the US Environmental Protection Agency (EPA), to estimate the theoretical risk of developing a malignant tumor as a result of exposure to the substance (ATSDR, 2005). For arsenic the oral slope factor is 1.5 (mg/kg)/day (EPA, 2012).

The equation for calculating cancer risk from exposure to water contaminants via ingestion is as follows (ATSDR, 2005): CR=EDxOSFx (EY/70); where, CR = expression of the cancer risk (unitless); ED = exposure dose [mg/kg/day]; OSF = oral slope factor [(mg/kg)/day]; EY = duration of exposure [years].

This calculation estimates a theoretical excess of cancer risk, expressed as the proportion of a population that can be affected by a substance capable of causing the development of a cancer, under the conditions of a fixed duration exposure, in our case, 15 and 30 years of exposure, relative to the average lifespan of 70 years. For example, an estimated cancer risk of 1×10^{-6} predicts the probability of a single additional cancer over background in a population of 1 million people (ATSDR, 2005).

Because of the conservative models used to derive risk factors, the use of this approach provides a theoretical estimate of risk, the actual risk is unknown and may even be zero, according to EPA (ATSDR, 2005). In the case of numerical risk estimates, it should be specified that risk factors are generated using mathematical models applied to epidemiological or experimental data for carcinogenic effects. Mathematical models extrapolate from large experimental doses to small environmental doses. Often, the experimental data represent exposures to chemicals in concentrations with orders of magnitude larger than those that can be found in the environment. In addition, these models often make the assumption that there is no threshold value for carcinogenic effects - a single molecule of a carcinogen is capable of causing cancer. (ATSDR, 2005)

Doses associated with this hypothetical estimated risk may be several orders of magnitude smaller than the doses reported in the scientific literature that would cause carcinogenic effects. As a result, an estimated cancer risk of less than 10^{-6} may indicate that toxicology data will advocate that an excess risk of cancer is more likely to be absent (ATSDR, 2005). An estimated cancer risk greater than 10^{-6}, requires careful review of toxicological data before we venture to assert that there is a potential cancer risk (ATSDR, 2005).

Although we must admit the usefulness of these numerical risk estimates in risk analysis, these estimates must par excellence be viewed in the context of the variables and assumptions involved in their derivation and in the broader context of biomedical opinions, genetic factors and not least, of the exposure conditions (ATSDR, 2005).

RESULTS AND DISCUSSION

Questionnaire data

Study sample characteristics are described in table 1. The study population's (n=25) distribution by gender was uneven, the majority (84%) being female and 16% male. The age and body weight (BW) distribution in the study sample was normal (Age: Kurtosis: -0.04; Skewness: -0.69; BW: Kurtosis: 0.13; Skewness: -0.70). None of the subjects had declared that metal processing or mining industry exists in the area of their residence.
The majority (84%) of the subjects stated that the source of water for drinking and cooking is tap water. 16% consume well water, 12% consume spring water with plain water, 24% consume bottled water, while 44% of subjects stated that they consume spring water with mineral water.

None of the investigated subjects currently smoke. 12% of the subjects smoked in the past, on average 9.33 ± 6.03 cigarettes/day (mean ± SD) for an average period of 11.67 ± 2.89 years (mean ± SD).

Regarding workplace exposure, one subject stated that he was exposed to pesticides and fertilizers, three subjects stated that they were exposed to chemical disinfectants and one subject to mofetic gas. Interviewed subjects stated that they were not exposed to arsenic, paints or solvents at their workplace.

The data obtained with the study questionnaire showed us that there is no metallurgical industry that involves the use of arsenic in Covasna, so this is not a source of exposure.

Table 1. *Study sample characteristics*

	Mean (%)	**SD**	**Range**
Female	(84%)	-	-
Male	(16%)		

Age (years)	59.40	12.38	28-77
Body weight (kg)	74.46	10.24	50-90
Education			
- Primary/professional	(44%)		
- High school/technical school	(39%)		
- University	(17%)		
Pollution sources near residence			
- Traffic	(56%)		
- Dye house	(8%)		
- Waste landfill	(8%)		
- Wood industry	(16%)		
Fuel for heating housing			
- Methane gas	(40%)		
- Wood	(44%)		
- Methane gas and wood	(16%)		
Fuel for cooking			
- Methane gas	(80%)		
- Wood	(4%)		
- Methane gas and wood	(16%)		
Source of water for drinking and cooking			
- Tap water	(84%)		
- Well water	(16%)		
- Spring water (plain water)	(12%)		
- Spring water (mineral water)	(44%)		
- Bottled water	(24%)		
Daily water ingestion (l/day)			
- Tap water (l/day)	5.03	6.87	0-25
- Spring water (mineral water) (l/day)	0.39	0.59	0-2
Consumption of game meat			
- Never	(88%)		
- 2-3 times a month	(8%)		
- once a week	(4%)		
Consumption of fish			
- Never	(56%)		
- 2-3 times a month	(28%)		
- once a week	(16%)		
Smoking			
- Current smoker	(0%)		
- Former smoker	(12%)		

Possible sources of exposure to arsenic in the studied area are: traffic, wood industry, burning of fossil fuels in homes, respectively consumption of spring water. Using body weight information, daily water consumption and drinking water source we were able to calculate the exposure dose and cancer risk individually for each study subject.

Water and nail samples

The average arsenic concentration measured in the nail samples collected from the subjects was 16.90 ± 20.97 µg/g (mean ± DS), with values ranging from 0.04 to 100.30 µg/g.

According to the US Agency for Toxic Substances and Disease Registry (ATSRD, 2013) arsenic levels in nails of unexposed people are ≤1 ppm (1 µg/g). Only one of the analzyed nail samples had arsenic levels below this level, therefore the results would suggest that the study population was chronically exposed to arsenic. However, it should be noted, that the mass of the samples was not sufficient to determine arsenic concentration by atomic absorption spectrometry with hydride generation, thus the concentrations obtained are higher than the actual level.

The average arsenic concentration measured in the water samples collected from the study area was 22.16 ± 37.44 µg/l (mean ± DS), with values between 0.5 µg/l and 91.8 µg/l.

Two of the samples had arsenic levels higher than the permissible limit of 10 µg/l (WHO, 2017). One of three samples was collected from the bathing water of the hospital's spa treatment facility, which is likely not consumed as drinking water, however there is the possibility of dermal exposure. The other sample with high arsenic level was collected from a spring used as drinking water.

Table 2 presents the results from the scientific literature regarding arsenic levels in water in Romania, compared with the results obtained in the present study.

The maximum arsenic concentration in water determined in the present study is lower than the maximum levels reported in the studies from Arad, Timis and Covasna County, but higher than the maximum levels reported in the studiues carried out in Bihor County.

Exposure doses and estimated cancer risk

Arsenic exposure doses via drinking water calculated for the study subjects based on arsenic concentrations measured in water samples collected from the study area, daily water ingestion and body weight declared by the subjects in the questionnaire, are presented in table 3.

Table 2. *Comparison of the results obtained with the results from the scientific literature*

	Arsenic levels in drinking water (µg/l)		
	Mean±SD	Min	Max
Present study, Covasna	**22.16 ± 37.44**	**0.5**	**91.8**
Gelmann et al. (2013), Arad	54.4 ± 27.0	-	-
Kunrath et al. (2013), Arad	40.2 ± 30.4	-	-
ASHRAM (Hough et al., 2010; Leonardi et al., 2012), Arad	-	0.1	196
Lindberg et al. (2006), Arad	0.70 (median)	-	95
Aposhian et al. (2000), Arad	-	2.8	161
Gurzau and Gurzau (2001), Bihor and Arad	-	0	176
ASHRAM Hough et al., 2010; Leonardi et al., 2012, Bihor	-	0.1	58
Lindberg et al. (2006), Bihor	0.48 (median)	-	24
Bloom et al. (2014), Timis	0.4 (median)	0	175.1
Neamtiu et al. (2015), Timis	8.6	0.5	175
Tudorache et al. (2011), Covasna	-	-	1505

Table 3. *Exposure doses calculated for arsenic levels measured in water samples*

	Arsenic exposure dose via drinking water (mg/kg/day)		
Drinking water source	**Mean ± SD**	**Min**	**Max**
Tap water	3.50E-05 ± 4.64E-05	0	1.56E-04
Spring water	9.26E-05 ± 1.79E-04	0	7.16E-04

According to ATSRD (2013) the minimal risk level (MRL) for acute oral exposure to arsenic is 0.005 (5.00E-03) mg/kg/day, calculated based on gastrointestinal effects, respectively the MRL for chronic oral exposure to arsenic is 0.0003 (3.00E-04) mg/kg /day, calculated based on dermal effects. Exposure doses calculated based on the tap water arsenic level did not exceed the MRL for acute and chronic exposure (ATSDR, 2013).

The exposure doses calculated based on the spring water arsenic levels were below the MRL for acute exposure, but in case of three subjects, the exposure dose exceeded the MRL for chronic exposure.

Cancer risks due to arsenic exposure through drinking water was estimated based on calculated exposure doses and are presented in table 4.

In case of exposure to the tap water arsenic levels for 15 years, the estimated cancer risks predict the probability of maximum 5 additional cancer cases over background in a population of 100,000 people. In case of exposure to the tap water arsenic levels for 30 years, the estimated cancer risks predict the probability of maximum one additional cancer case over background in a population of 10,000 people.

Table 4. *Cancer risks estimated based on arsenic exposure doses*

Drinking water source	Exposure period (years)	Mean ± DS	Max
Tap water	15	1.12E-05 ± 1.49E-05	5.02E-05
	30	2.25E-05 ± 2.98E-05	1.00E-04
Spring water	15	2.97E-05 ± 5.73E-05	2.30E-04
	30	5.95E-05 ± 1.15E-04	4.60E-04

The cancer risks calculated for the exposure to arsenic levels in spring water, predict the probability of maximum of 3 additional cancer cases over background in a population of 10,000 people, in the case of an exposure for 15 years, respectively the probability of maximum 5 additional cancer cases over background in a population of 10,000 people, in case of an exposure for 30 years.

The cancer risks estimated in this study were greater than 10^{-6}, which according to the scientific literature in this field (ATSDR, 2005; WHO, 2010; EPA, 2012) suggests that there is a potential excess risk of cancer, but the results must be viewed in the context of the variables and the assumptions involved in deriving them and in the context of the exposure conditions described for this study.

CONCLUSION

The groundwater sources in Covasna, Romania represent a potential health hazard for the population in the area and there is a potential risk of affecting the health of the population, however, due to the limitations of this study, further studies are needed with extended number of participants, more environmental and biological samples and additional individual data.

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