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Arsenic in drinking water and congenital heart anomalies in Hungary

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ABSTRACT

Inorganic arsenic can get easily through the placenta however there are very few human data on congenital anomalies related to arsenic exposure. Objective of our study was to explore the associations between arsenic content of drinking water and prevalence of some congenital anomalies. Four anomalies reported to the Hungarian Congenital Anomalies Registry between 1987 and 2003 were chosen to be analysed in relation to arsenic exposure: congenital anomalies of the circulatory system ($n = 9734$) were considered as cases, while Down syndrome, club foot and multiple congenital malformations were used as controls ($n = 5880$). Arsenic exposure of the mothers during pregnancy was estimated by using archive measurement data for each year and for each settlement where the mothers lived. Analysis of the associations between the prevalence of congenital heart anomalies and arsenic exposure during pregnancy was performed by logistic regression. The child's gender and age of the mother were adjusted for. The associations were evaluated by using the present EU health limit value of 10.0 μg/L arsenic concentration as a cut-off point. Regular consumption of drinking water with arsenic concentration above 10 μg/L during pregnancy was associated with an increased risk of congenital heart anomalies in general (adjusted OR = 1.41; 95% C.I.: 1.28–1.56), and especially that of ductus Botalli persistens (adjusted OR = 1.81, 95%C.I.: 1.54–2.11) and atrial septal defect (adjusted OR = 1.79; 95%C.I.: 1.59–2.01). The presented results showed an increased risk of congenital heart anomalies among infants whose mothers were exposed to drinking water with arsenic content above 10 μg/L during pregnancy. Further studies of possible similar effects of concentrations below 10 μg/L are warranted.

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Introduction

More than one hundred million people worldwide are at risk of elevated arsenic exposure (Vahter, 2009). Hungary has also been struggling with the health risks of high arsenic level in the drinking water for the last decades. (Csanády et al., 1985; Leonardi et al., 2012; Rudnai et al., 2013) It has been widely accepted that arsenic exposure via drinking water is associated with excess risk of skin, lung, bladder and kidney cancer. According to data from animal experiments inorganic arsenic can easily get through the placenta and cause serious teratogenic effects.

Inorganic arsenic proved to be teratogenic in mice (Baxley et al., 1981; Morrissey and Mottet, 1983; Nagymajtényi et al., 1985; Wlodarczyk et al., 1996), rats (Beaudoin, 1974) and hamsters (Carpenter, 1987; Ferm and Hanlon, 1985; Hood and Harrison, 1982; Willhite, 1981) following oral, parenteral or inhalational exposure. Congenital disorders varied depending on the arsenic dosage and gestation period.

The major teratogenic effects induced by inorganic arsenic observed in animal experiments were neural tube defects and similar disorders of the cephalic neural folds. The minor disorders that could be observed due to arsenic exposure were fused ribs, renal agenesis, micromelia, facial malformations, twisted hindlimb, anophthalmia and microphthalmia (WHO, 2001)

Human placental transfer of arsenic was indicated by increased frequency of spontaneous abortion, still birth and perinatal death among those exposed to drinking water with high arsenic level during pregnancy (Ahmad et al., 2001; ATSDR, 2007; Bloom et al., 2010; Börzsönyi et al., 1992; Hopenhayn-Rich et al., 1999; Milton et al.,

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2005; Rahman et al., 2007; Rudnai et al., 2006, 2013; von Ehrenstein et al., 2006).

Very few studies have been published, however, with findings on possible associations between arsenic content of drinking water and congenital anomalies in humans (Dorsch et al., 1984; Engel and Smith, 1994; Kwok et al., 2006; Nordström et al., 1979; Orr et al., 2002; Wu et al., 2011; Zierler et al., 1988). Out of the mentioned ones only two papers reported about increased risk of congenital heart anomalies (Engel and Smith, 1994; Zierler et al., 1988) in areas supplied with drinking water with high arsenic content though the reported levels of arsenic were not unequivocal. Heart anomalies are the second most frequent congenital defects in Hungary (Susánszky and Czeizel, 1989). The database of the Hungarian Congenital Abnormality Registry (HCAR) and the archive measurement results of arsenic concentrations of drinking water in settlements all over Hungary provided a unique opportunity to study the associations between the prevalence of congenital heart anomalies (CHA) and the arsenic level of drinking water supplied to the settlements where the mothers lived during pregnancy.

Methods

Studied health outcomes

The Hungarian Congenital Abnormality Registry was established as the first country-wide registry in the world in 1962. (Métneki et al., 2013). Since then it has been collecting and evaluating the data and reports in the whole country on congenital anomalies of newborn babies and infants observed during the first year of life either by the obstetricians or the paediatricians. We used a part of this database covering a period of 17 years between 1987 and 2003. Out of the registered congenital disorders we chose four anomalies to be analysed in relation to arsenic exposure: congenital anomalies of the circulatory system (International Classification of Diseases, ICD-10 codes: Q20.0–Q28.9) were considered as cases ($n = 9734$), while Down syndrome (trisomia, Q90.0–Q90.9), club foot (talipes equinovarus, Q66.0) and multiple congenital malformations (Q89.7) were used as controls ($n = 5880$). As most of the congenital disorders of the circulatory system relate to the heart, for practical reasons we use "congenital heart anomalies (CHA)" in this sense. In order to eliminate any disturbing "noise", data of children with overlapping both case and control diagnoses (especially Down syndrome and multiple congenital malformations) were transformed to "missing". The following pieces of information were also taken into consideration: the child's gender, year of birth, the mother's year of birth, place of living, postal code and further diagnoses (up to 10). Unfortunately, information on gender of the child was missing in 48 cases (0.5%) and 281 controls (4.8%) and age of the mother in 42.9% of the cases and 25.3% of the controls (Table 1).

Exposure estimation

In the frame of the National Database of Drinking Water Quality, arsenic measurements were started from 1981 first by a semi-quantitative screening method and later by systematic measurement programmes using samples taken simultaneously by the local public health institutions at several points of the settlements and determined in 12 centrally controlled laboratories (Csanády et al., 1985). Step by step, more and more settlements were covered by arsenic measurement results. Some waterworks using deep well waters with high arsenic content started to implement drinking water quality improvement programmes from 1986 on, therefore water quality in settlements of their distribution system changed in the course of time and was repeatedly sampled. However, these results were stored in several locations, mostly on paper files.

Table 1
Characteristics of the study population.

Variables	Controls		Cases[a]											
			Total		Ventricular septal defect		Atrial septal defect		Ductus Botalli persistens		Pulmonary artery anomalies		Other anomalies	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Gender														
Male	3271	58.4	4744	49.0	1959	46.6	1245	45.7	665	48.3	426	48.1	1272	55.0
Female	2328	41.6	4942	51.0	2249	53.4	1480	54.3	713	51.7	460	51.9	1039	45.0
Mother's age														
n	4180		5531		2560		1784		803		458		1082	
Mean (±s.d.)	27.7 (±6.6)		26.8 (±5.6)		26.6 (±5.6)		27.1 (±5.7)		27.2 (±5.6)		26.9 (±6.0)		26,9 (±5.6)	

[a] More than one anomaly per child is possible.

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