RESEARCH REPORT

Geochemistry of ground water and the incidence of acute myocardial infarction in Finland

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Study objective: To examine the association of spatial variation in acute myocardial infarction (AMI) incidence and its putative environmental determinants in ground water such as total water hardness, the concentration of calcium, magnesium, fluoride, iron, copper, zinc, nitrate, and aluminium.

Design: Small area study using Bayesian modelling and the geo-referenced data aggregated into 10 km×10 km cells.

Setting: The population data were obtained from Statistics Finland, AMI case data from the National Death Register and the Hospital Discharge Register, and the geochemical data from hydrogeochemical database of Geological Survey of Finland.

Participants: A total of 18 946 men aged 35–74 years with the first AMI attack in the years 1983, 1988, and 1993.

Main results: One unit (in German degree °dH) increment in water hardness decreased the risk of AMI by 1%. Geochemical elements in ground water included in this study did not show a statistically significant effect on the incidence and spatial variation of AMI, even though suggestive findings were detected for fluoride (protective), iron and copper (increasing).

Conclusions: The results of this study with more specific Bayesian statistical analysis confirm findings from earlier observations of the inverse relation between water hardness and coronary heart disease. The role of environmental geochemistry in the geographical variation of the AMI incidence should be studied further in more detail incorporating the individual intake of both food borne and water borne nutrients. Geochemical-spatial analysis provides a basis for the selection of areas suitable for such research.

Cardiovascular disease (CVD) is the major cause of death in most developed countries including Finland.[1–3] The occurrence of coronary heart disease (CHD) varies between populations[1 4] but also within populations inside a country.[5] Already in 1947 Kannisto found that CHD mortality was much higher in the eastern part than in the western part of Finland. In the 1980s the CHD risk was still 40% higher in eastern Finland than that in western and southern parts of the country.[6] The major CHD risk factors do not fully explain the geographical variation of CHD risk in Finland.[7–9] Although the geographical differences have long been known, the reasons are still partly ambiguous.[10] Besides a genetic predisposition[11–13] several lifestyle and environmental factors have been implicated in the pathogenesis of CHD.[14–16] Availability of trace elements in soil and ground water may be a cause of certain chronic ailments.[17] Soils and rocks in the countries of northern Europe are poor sources of many essential trace elements.[17 18]

Our recent study of the spatial distribution of the first acute myocardial infarction (AMI) event showed that despite the decreasing trend in AMI incidence, the geographical difference in incidence and high risk areas has remained within Finland.[19] The presence of high risk areas for AMI suggests that genetic or environmental risk factors have accumulated in certain geographical locations in Finland. Our aim was to examine the possible association of spatial variation of AMI incidence with geochemical compounds in ground water.

METHODS

Finnish ground water is slightly acidic and very soft (1–4°dH) or soft (4–8°dH).[20] Besides the geological factors affecting trace element composition, atmospheric, anthropogenic, and marine factors also contribute to the chemical composition of the ground water.[21]

The data on men aged 35–74 years with the first attack of AMI (18946 cases) were obtained from the nationwide Death Register and the Hospital Discharge Register. The national personal identification number was used to perform a computerised records linkage of the data for deaths and hospitalisation attributable to AMI (ICD-8 and ICD-9 codes 410–414). Both fatal and non-fatal events from the years 1983, 1988, and 1993 were included in the study. Cases with a previous hospitalisation for AMI were excluded. Data for these three years have been pooled. The data on population at risk, provided by coordinates of the place of residence, were obtained from Statistics Finland. The data were aggregated into 10 km×10 km grid cells to ensure the protection of privacy of the individuals.

Geochemical data were obtained from the hydrogeochemical database of the Geological Survey of Finland.[21] The data on total water hardness (°dH), Ca, Mg, Fe, F^-, NO_3^- (mg/l) and Cu, Zn, and Al (μg/l) were available. Element concentrations were determined with different methods, for example, ICP-MS, ICP-AES, iconography, and AAS. The original data contained from 3621 up to 12 407 ground water samples.

The geochemical data were interpolated into a regular grid by using the ALKEMIA software developed at Geological Survey of Finland.[22] In the ALKEMIA Smooth interpolation method, the nearest samples to the grid cell receive greater

Abbreviations: CVD, cardiovascular disease; AMI, acute myocardial infarction; CHD, coronary heart disease weight. The value of the cell is a weighted median of sample values.[23–26]

Bayesian spatial conditional autoregressive model (CAR) with covariates, which is currently in wide use in the field of the disease mapping, was applied in this study.[27–30] Because Finland is sparsely inhabited, we propose one modification, which is pertinent to the sparsely populated areas. In the case of the 10 km×10 km grid over Finland (excluding Lapland), some grid cells are empty and have to be omitted from the analysis; thus 5% of cells would be omitted. However, once we take environmental factors into account, assuming that the disease risk is influenced by both demographic factors (that is, people who actually live within the grid cell) and environmental factors in each cell whether or not it is inhabited, the omission of unpopulated cells results in a loss of information. The covariates included in the model were the age of onset of AMI and the levels of geochemical compounds in the ground water. The following modification is thus proposed.

Let Y_{ik} denote the number of cases in the cell i and age group k. Furthermore, let N_{ik} denote the respective population at risk. The proposed probability distribution is then as follows:

$$P(Y_{ik}=y|N_{ik},\mu_{ik})=\begin{cases}\dfrac{e^{-N_{ik}\mu_{ik}}(N_{ik}\mu_{ik})^{y}}{y!} & \text{if } 0\le y\le N_{ik}\\ 0 \text{ elsewhere}\end{cases}$$

that is, the Poisson distribution is assigned to the inhabited cells and the uninhabited cells naturally have no cases of the disease with the unit probability. Also we assign common regression structure to the μ_{ik}:

$$\log(\mu_{ik})=\alpha+\lambda_i+\beta_k+\xi Z_i+\log(N_{ik}) \text{ if } N_{ik}>0$$
$$\log(\mu_{ik})=\alpha+\lambda_i+\beta_k+\xi Z_i \text{ if } N_{ik}=0$$

where
α, is the baseline risk
λ_i, is the local unexplained spatial random effect
β_k, is the effect of age group k on the risk level
K, is the age group, $k=0,\ldots,K$
ξ, is a vector of environmental covariate effects
Z_i, is a vector of environmental covariates for area i

In this analysis, the age axis was divided into eight, five year age groups: 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–74. A non-proportional hazard model described their effect, which for AMI is more appropriate than the proportional hazards.

As outlined in the preceding section seven geochemical covariates were included in the analysis.

The regression coefficients β and ξ were given non-informative Normal priors N(0,0.00001), the background level α was given an improper flat prior

$$p(\alpha)\propto 1$$

and the λ were given a CAR structure:

$$\lambda_i \sim N(\overline{\lambda_{-i}},\tau m_i)$$

where
λ_{-i}, are spatial variation parameters in the neighbourhood of i
m_i, is the number of neighbors for cell i
τ, is the overall level of spatial precision (inverse spatial variation)

In the CAR models a neighbourhood structure needs to be defined. The neighbours were defined to be all those cells adjacent to the cell i through side or corner. Thus each cell could have at most eight (8) neighbours.

The model was fitted using WinBUGS. A total of 10000 iterations with 5000 burn-in were run. ''Burn-in'' denotes iterations, which were discarded because of non-convergence of the model at the early stages of the algorithm. The evaluation of the test results showed that a satisfactory convergence was reached.

The posterior joint and marginal distributions of the parameters of interest were estimated and summarised. The p% highest density regions (HDR), defined as most compact set of parameter values the posterior density mass over which is p/100, is used in Bayesian statistics to describe the variability of the estimate. It is thus by its nature somewhat similar to the frequentist confidence interval.

RESULTS

Age group and the total water hardness, Ca, Mg, Fe, F^-, Cu, Al, Zn, and NO_3^- concentrations in the ground water were included in the analyses as covariates. The overall age adjusted incidence of AMI among men aged 35–74 year was 480/100 000/year (posterior 95% HDR 473, 487). Table 1 gives information on the chemical contents of ground water. Table 2 illustrates the number of AMI cases, population at risk, and AMI incidence by age and water hardness. One unit (°dH) increment in water hardness decreased the risk of AMI by 1% (table 3). The levels of other geochemical elements included in this study did not have any additional effect on the spatial variation of the incidence of AMI.

DISCUSSION

The large geographical variation and changes in the incidence of AMI in Finland cannot be explained by individual lifestyle or genetic factors alone; environmental exposures must also contribute to the development of the disease. The classic risk factors and socioeconomic status provide only a partial explanation for the excess CHD risk in eastern Finland.[7 31] The age distribution of the population did not have an effect on the geographical variation of the incidence of AMI. The results support the early observations of the inverse relation between the AMI incidence and total water hardness. An

Table 1 Geochemical concentrations in ground water in Finland

Element	Median	Mean	SD	25%	75%	Number
Water hardness (°dH)	2.8	3.8	10.0	1.3	4.9	3621
Ca (mg/l)	14.4	19.9	67.3	6.9	24.4	3621
Mg (mg/l)	3.3	4.8	5.6	1.5	6.5	3621
Zn (μg/l)	11.4	51.4	231.8	3.9	36.8	3621
Al (μg/l)	10.4	88.1	310.7	1.7	61.4	3621
Cu (μg/l)	2.4	14.5	41.9	0.6	9.8	3621
F^- (mg/l)	0.1	0.4	0.6	0.1	0.3	12407
Fe (mg/l)	0.0	0.3	1.4	0.0	0.1	3621
NO_3^- (mg/l)	1.0	5.8	12.1	0.2	5.9	4039

Table 2 Number of AMI cases, population at risk, and the AMI incidence per year by age and water hardness among 35 to 74 year old men in Finland in 1983, 1988, and 1993 (pooled data)

	Water hardness (°dH)								
	<1.7	(n = 688)		1.71<=<5.2	(n = 1389)		⩾5.2	(n = 692)	
Age	AMI cases	Population at risk	AMI incidence	AMI cases	Population at risk	AMI incidence	AMI cases	Population at risk	AMI incidence
35–39	49	68730	71.3	282	506395	55.7	9	17615	51.1
40–44	124	62520	198.3	675	468014	144.2	20	16430	121.7
45–49	180	55485	324.4	1144	409953	279.1	47	14447	325.3
50–54	332	50500	657.4	1662	350975	473.5	63	12443	506.3
55–59	447	51842	862.2	2446	341606	716	71	12189	582.5
60–64	487	52081	935.1	2820	333483	845.6	97	12030	806.3
65–69	533	47996	1110.5	3139	306651	1023.6	101	11402	885.8
70–74	606	42334	1431.5	3181	271337	1172.3	105	10394	1010.2
Age standardised	2758	431488	562.1	15349	2988414	469.5	513	106950	437.6

Table 3 Estimated effects of the geochemical covariates on the incidence of the first AMI among 35–74 year old Finnish men in 1983, 1988, and 1993 (pooled data)

Element	Posterior mean	95% HDR (high density region)
Total water hardness (°dH)*	−0.0097	−0.0214 to −0.0003
Zn (μg/l)	−0.0007	−0.0061 to 0.0048
Al (μg/l)	−0.0003	−0.0007 to 0.0002
Cu (μg/l)	0.0401	−0.0653 to 0.1477
F^- (mg/l)	−0.0317	−0.1453 to 0.0899
Fe (mg/l)	0.1015	−0.1298 to 0.3176
NO_3^- (mg/l)	0.0006	−0.0004 to 0.0016

*Statistically significant effect. For example, one unit increment of Cu on average increases the AMI risk by 4% (posterior mean = 0.0401).

inverse relation between water hardness and CVD mortality has been detected in several studies.[32–37] They have suggested that CHD mortality can be related to the amount of magnesium and calcium in drinking water.[36 38–44] In some studies an association between CVD and water hardness was not found.[45–48] Much of the disagreement in earlier studies may be related to the complexity of the ecological analysis and the difficulty to apply results from ecological studies at the individual level.

In the general population, the magnesium intake has decreased over the years especially in the western world.[49] Some previous studies have shown that a large number of subjects had a lower intake of magnesium than the recommended dietary amount (350 mg/day).[42] It has been suggested that magnesium in water, appearing as hydrated ions, has a higher bioavailability than magnesium in food, which is bound in different compounds that are less easily absorbed.[50]

Fluoride concentrations of around one mg/l in household water may be beneficial.[40 41] Recent studies have also provided evidence that high serum iron and copper concentrations are associated with the CHD.[51 52] In this study one mg/l increment in the fluoride concentration in the drinking water was associated with a 3% decrease in the risk of AMI. In our study one μg/l increment in copper and one mg/l increment in iron on average increased the risk of AMI by 4% and 10%, respectively. The differences were not, however, statistically significant. The non-significant results in our study may be attributable to excessive smoothing technique. Thus, our study provides further supportive evidence for the importance of the ground water fluoride, iron and, copper concentrations for the risk of AMI.

CHD has a multifactorial aetiology. The method of spatial analysis used in this study is especially useful for testing the impact of several factors simultaneously. The validity of the Bayesian method used in this study has been also demonstrated earlier studies.[19 27 53] Additional simulations have been run to check the validity of the proposed changes to it regarding the inclusion of the uninhabited cells in the analysis.

Ground water reflects the contents of trace elements in soil and bedrock[21 54] but only a small proportion of the population use locally produced food supplies, cereals, and vegetables. Individual studies on the role of intake of both food and water-borne nutrients should incorporate environmental exposure or control for it.

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