Drinking Water and Risk of Stroke
The Hidden Element

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“There are more things in heaven and earth, than are dreamt of in your philosophy.”
—William Shakespeare, “Hamlet,” Act 1, Scene 5

Less than 1% of the fresh water (approximately 0.007% of all water on earth) is accessible for direct human use. We use this small amount of water for drinking, transportation, heating and cooling, industry, and many other purposes. In countries with limited access to safe drinking water (and also in developed countries with an increasing consumption of bottled mineral water), its cost has been rising. Furthermore, the price per liter of bottled water may be surprisingly higher than the price of a liter of gasoline! For example, the average cost of regular gasoline (87 octanes) is US $0.8 to 1.1 in the United States and Canada, and 1.7 to 1.9 Euros in European countries (Belgium, France, The Netherlands, Germany, Italy, and the United Kingdom according to the European Commission, Oil Bulletin, Weekly Report, April 2010). By contrast, the average price of a liter of bottled water (2×500 mL) in convenience stores in North America (United States, Canada) range from US $2 to 3 and 2 Euros in some European countries.

Toxic Metals in Drinking Water?
Arsenic is a toxic metal usually found in natural environments. Humans can be exposed to arsenic through inhaling air, eating food, and/or drinking water. Most food arsenuclals are organic and have little or no toxicity, whereas arsenic exposure from drinking water sources is an inorganic form occurring at relatively higher doses (eg, hundreds of micrograms per day). Therefore, the most common cause of human toxicity is from contamination of drinking water in areas with higher arsenic content (ie, natural sources, mining, industrial or agricultural sources [pesticides or fertilizers]). Arsenic concentration in bottled water is usually <1 µg/L.

Chronic arsenic exposure has been associated with an increased risk of cancer (urinary tract, lung, skin), gastroenteritis, myocardial infarction, and peripheral neuropathy. Drinking water contaminated with arsenic has been found in both developed and developing countries. According to the World Health Organization, arsenic contamination of ground water has been found in many countries, including Argentina, Bangladesh, Chile, China, India, Mexico, Thailand, and the United States (www.who.int/water_sanitation_health/publications/facts2004/en/index.html).

Interestingly, limited information is available on the association between low to moderate arsenic exposure through drinking water (<300 µg/L) and cardiovascular diseases. Studies in different areas from the United States showed some inconsistent findings.

Findings
In the present issue of Stroke, the authors investigate the association between low-level arsenic exposure in drinking water and the ischemic stroke admissions in Michigan. They found that even low exposure to arsenic is associated with an increased incident risk of stroke (relative risk, 1.03; 95% CI, 1.01 to 1.05 per µg/L increase in arsenic concentration). The authors also compared whether that exposure was associated with other nonvascular conditions (hernia, duodenal ulcer) not expected to increase their risk. Comparing zip codes in Genesee County at the 90th percentile of arsenic levels (21.6 µg/L) with those at the 10th percentile (0.30 µg/L), there was a 91% increase in risk of stroke admission (relative risk, 1.91; 95% CI, 1.27 to 2.88). The results were consistent in showing an increased risk for stroke, but not for other control medical conditions (hernia and duodenal ulcer). Moreover, they found a graded effect: a higher incident risk among those individuals exposed to higher water concentrations of arsenic (Figure 2).

Does Arsenic Exposure Cause Stroke?
The answer to this question may not be easy. To establish causality in medicine requires proof of some criteria (ie, strength of association, consistency, specificity, temporality, biological gradient, and biological plausibility, among others) originally described by Austin Bradford Hill, Professor of Medical Statistics (Table). As described in the present article, the authors were able to report on the strength of the association for stroke (relative risk, 1.03; 95% CI, 1.01 to 1.05 per µg/L increase in arsenic concentration). Similar findings were described for cardiovascular mortality. Other studies described a gradient effect for cerebral infarction after adjusting for confounders (OR, 1.0, 3.4, 4.5, and 6.9, respectively, for those who consumed...
Table. Criteria for Judgment of Causal Associations

1) Temporal sequence
   Did exposure precede outcome?

2) Strength of association
   How strong is the effect measured as relative risk or OR?

3) Consistency of association
   Has effect been seen by others?

4) Biological gradient (dose–response relation)
   Does increased exposure result in more of the outcome?

5) Specificity of association
   Does exposure lead only to outcome?

6) Biological plausibility
   Does the association make sense?

7) Coherence with existing knowledge
   Is the association consistent with available evidence?

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water with an arsenic content of 0.0, 0.1 to 50.0, 50.1 to 299.9, and >300 µg/L).15 The association between arsenic exposure is specific not only for cardiovascular disease, but also for different cancers.16,17 Regarding the biological plausibility, several epidemiological studies suggest that the exposure correlates with endothelial dysfunction, increased of the oxidative stress, and increased incidence of atherosclerosis, a common pathway for the development of cardiovascular disease.8,18

What Are the Limitations Concerning This Study?

As recognized by the authors, the present study has several limitations, including the lack of individual-level data, ecological design, unknown timing of exposure, and the role of unmeasured confounders. As such, its results should not be used to infer a causal relationship between arsenic and ischemic stroke. However, the findings of this study are hypothesis-generating.

In summary, some environmental factors such as arsenic exposure in drinking water may increase the incident risk of myocardial infarction, stroke, and cardiovascular mortality.14,15 The increased risk of ischemic stroke may occur with exposure to low arsenic concentrations in drinking water. The effect may be higher in individuals with some genetic predisposition and for those with known vascular risk factors (smoking, hypertension, diabetes, etc).18 No specific treatment of proven benefit is currently available to treat chronic arsenic toxicity. Treatment is usually limited to supportive measures and to eliminate the exposure. Considering that two thirds of strokes occur in developing countries with lower access to safe drinking water, governments and policymakers should be aware of this worldwide problem to optimize controls, adjust filtration processes, facilitate access, and improve the quality of one of the most vital elements on earth for human survival: water.

Disclosures

G.S. received salary support from the Clinician–Scientist Award from the Heart and Stroke Foundation of Ontario.

References


Key Words: arsenic, brain infarction, cerebral infarct, outcomes, toxic, water.
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*Stroke*. 2010;41:2451-2452; originally published online October 14, 2010;
doi: 10.1161/STROKEAHA.110.596395

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