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Lithium in the Public Water Supply and Suicide Mortality in Greece

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Abstract The purpose of the present study was to evaluate the association between lithium levels in the public water supply and prefecture-based suicide rates in Greece. Analyses were conducted with respect to lithium levels in 149 samples from 34 prefectures of Greece. The average lithium level was 11.10 μg/l (range 0.1 to 121 μg/l). The results indicate that there is a tendency for lower suicide rates in the prefectures with high levels of lithium in drinking water. Ecological studies explained by researchers Schrauzer and Shrestha have revealed the existence of statistically significant inverse associations between the lithium levels in drinking water and the incidence of suicides, homicides, rapes, possession of narcotic drugs, and in juveniles, the rates of runaway from home. Such a result of inverse relationship was not proven by Kabacs et al., most likely because the differences of the lithium levels in the selection of their case–control samples were not large enough. In addition, probably the selection of random regions in Japan and East England might have been biased. Thus, the addition of small amounts of lithium to the drinking water could provide an effective means to lower the incidence of these conditions in the general population. Furthermore, the nutritional importance of lithium in the form of the carbonate named lithium carbonate (Li_2CO_3) is currently still viewed primarily as a pharmacological agent. The study by Al-Chalabi et al. state that the therapeutic activity of lithium in amyotrophic lateral sclerosis (ALS) is worth investigating. Any drug that can be shown to slow the course of ALS in a clinically significant way and to be safe and well tolerated will be an important advance for patients with this disease.

Keywords Mental health · Lithium · Tap water · Greece · Suicide · Signaling pathways · Development · Mood disorders · Mood stabilizer

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Introduction

Some studies have shown an association between low lithium intakes from water supplies and suicide as well as homicide rate [1].

Using data from 27 Texas counties for the period 1978–1987, Schrauzer and Shrestha [2] found that the incidence rates of suicide, homicide, and rape were significantly higher in counties whose drinking water supplies contain little or no lithium than in counties with water lithium levels ranging from 70 to 170 μg/l. Ohgami et al. [3] examined lithium levels in tap water in the 18 municipalities of Oita prefecture in Japan in relation to the suicide standardized mortality ratio in each municipality. They found that lithium levels were significantly and negatively associated with suicide standardized mortality ratio averages for the period 2002–2006 and suggested that

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even very low levels of lithium in drinking water may play a role in reducing suicide risk within the general population. Similarly, Kapusta et al. [4] evaluated the association between local lithium levels in drinking water and suicide mortality at district level in Austria. The overall suicide rate as well as the suicide mortality ratio were inversely associated with lithium levels in drinking water and remained significant after sensitivity analyses and adjustment for socioeconomic factors. Recently, Blüml et al. [5] evaluated the association between lithium levels in the public water supply and county-based suicide rates in 226 Texas counties, with a state-wide sample of 3,123 lithium measurements from the public water supply. The findings provided evidence that higher lithium levels in the public drinking water are associated with lower suicide rates. However, Kabacs et al. [6] did not prove this association between lithium in drinking water and suicide rates across the East of England for the period 2006–2008.

No association was found when measuring of lithium levels in tap water in the 47 subdivisions of the East of England in this study of Kabacs and the correlation of these with the suicide standardized mortality ratio in each subdivision. The results of this study suggest that in the southeastern parts of Austria, psychiatrists coincidently exhibit a significant negative relationship with suicide mortality with lithium levels in water, which may be an argument for an influence of local lithium prescriptions by psychiatrists on lithium levels in drinking water. According to the previous findings, the purpose of the present study was to evaluate the association between lithium levels in the public water supply and prefecture-based suicide rates in Greece.

Method

A total of 149 samples of drinking water were collected during the last trimester of 2012 from 34 out of 52 prefectures of Greece from both rural and urban areas. Lithium levels were analyzed by inductively coupled plasma mass spectrometry (ICP-MS) at *Center of Biological Research of Armed Forces* (Stefansson et al. 2007). The Greek Statistic Authority provided a database of suicides by gender for the period from 1999 to 2010 at the prefecture level (Greece is divided in 52 prefectures). The average standardized suicide rates have been calculated by analysts (number of suicides per 100,000 population) for each prefecture for the period 1999–2010. The analysis was performed with the statistical package IBM SPSS 20.

Results

Analyses were conducted with respect to lithium levels in 149 samples from 34 prefectures of Greece. The average number of samples per prefecture was 4.72 (range 1–17). Values were calculated for lithium in drinking water by prefecture. The highest level for lithium is located in the prefecture of Samos island (121 μg/l) and the lowest price in the prefecture of Chios island (0.1 μg/l). The average lithium level, as evidenced by the raw values for the 34 prefectures of Greece, was 11.10 μg/l (SD=21.16). In parallel, the analysis of 21 samples of different kind of bottled waters of Greece showed that their mean lithium levels was 6.21 μg/l (SD=16.35).

We set the values above 2 SD of the mean bottled waters' lithium levels with the value 32 μg/l. Linear regression analysis was performed to predict the standardized suicide rates by lithium values per prefecture.

A linear regression was conducted (enter method) to test the prediction of suicides per 100,000 residents by lithium values in drinking water. The R^2 was equal to 0.03 and adjusted R^2 was equal to 0.02. Accordingly, 2 % of the variance of suicides in prefecture level could be interpreted by the effect of the independent factor. *The slope of the regression* line is significantly *different* from zero $F(1.147)=4.41$, $p<0.05$. Judging from the coefficient of regression, we found that the independent variable significantly contributes to the prediction of the dependent variable ($\beta=-0.17$, $t=-2.10$, $p<0.05$). The results indicate that there is a tendency for lower suicide rates in the prefectures with high levels of lithium in drinking water (see Table 1 and Fig. 1).

Discussion

Some earlier investigations indicated that lithium, as a substance occurring naturally in food and drinking water, may exert positive effects on mental health [2]. We found that suicide mortality was inversely associated with lithium levels of drinking water in the 34, out of 52, prefectures of Greece we studied. Similar results were found in Japan [3], Austria [4], and Texas, [5] but not in East England [6].

Lithium is found in variable amounts in grains and vegetables, while drinking water also provides significant amounts of that element. Human dietary lithium intakes vary over a wide range and depend on location and the type of foods consumed. The evidence indicates an intake of 1,000 μg/day for an adult of 70 kg. In studies conducted from the 1970s to

Table 1 Linear regression for the prediction of standardized mean rate of suicides (1999–2010), per 100,000 residents, at prefecture level by the values of lithium in drinking water

Predictor	B	SE B	Beta
Values of lithium in drinking water*	−0.02	0.01	−0.17*

Dependent variable: mean prefecture suicide rate (period1999–2010), per 100,000 residents (method enter) $R^2=0.03$ $F(1.147)=4.41$, $p<0.05$

*$p<0.05$

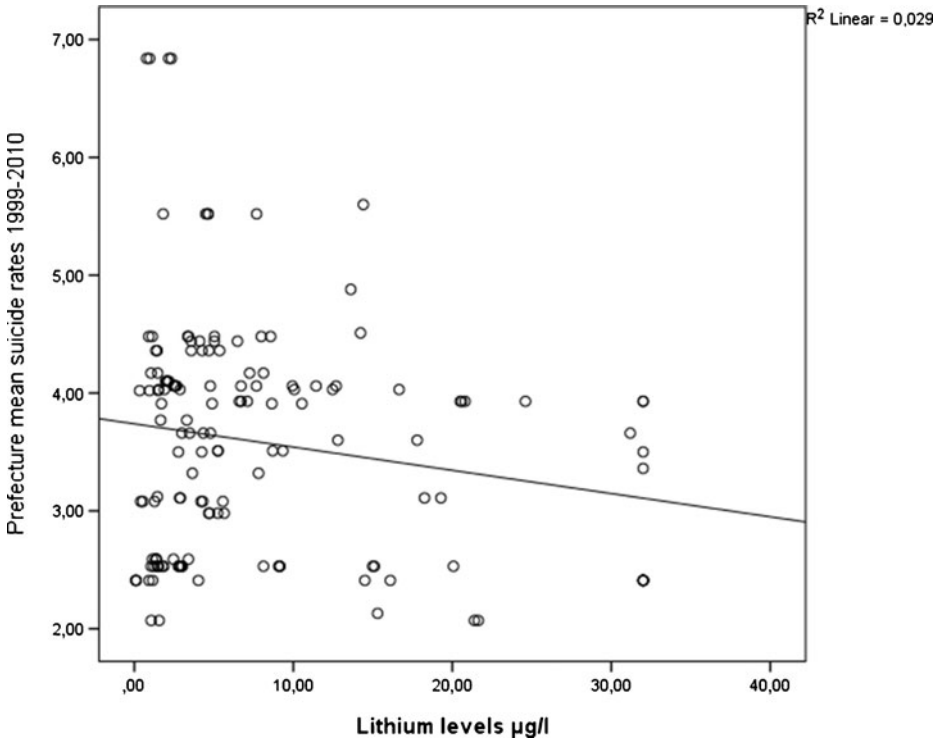

Fig. 1 Scatter plot of lithium values in micrograms per liter and standardized mean rate of suicides per prefecture for the years 1999 to 2010

the 1990s, rats and goats maintained on low-lithium rations were shown to exhibit higher mortalities as well as reproductive and behavioral abnormalities [1]. The biochemical mechanisms of action of lithium appear to be multifactorial and intercorrelated with the functions of several enzymes, hormones, and vitamins, as well as with growth and development. For example, a significant direct association was observed between hair lithium and cobalt concentrations, which suggests a role of lithium in the transport and distribution of vitamin B12 [7]. Lithium appears to play an especially important role during the early fetal development as evidenced by the high lithium contents of the embryo during the early gestational period. A recent study showed that the exposure to lithium may exert antiaging capabilities and unambiguously decreases mortality in evolutionary distinct species [8]. However, exposure to lithium via drinking water and other environmental sources may affect thyroid function, consistent with known side effects of medical treatment with lithium [9]. It has been shown that lithium plays an important role in embryogenesis, with biochemical mechanisms of action related to the function of many enzymes, hormones, vitamins, and growth factors. Specifically, lithium exerts neurotrophic activity and is involved activity in inhibiting the biochemical pathway, e.g., GSK-3b and Wnt.

The beneficial effect of lithium can be explained through its contribution in reducing glial inflammation, increasing pre- and postsynaptic protein, and reducing stress which causes structural and functional damage to the dendrites [10].

Although lithium is known to prevent suicide in people with mood disorders, it is uncertain whether lithium in drinking water could also help lower the risk in the general population. It is known that in therapeutic doses, which are more than 100 times higher than natural daily intakes, lithium has been proven to be a mood stabilizer and suicide preventive. According to the arachidonic acid (AA) cascade hypothesis, the brain AA cascade is a common target of lithium, as well as other mood stabilizers, and that bipolar symptoms are associated with an upregulated cascade and excess AA signaling via D2-like and NMDA receptors [11]. Zarse et al. indicate that low-dose Li^+ exposure causes reduced mortality in *Caenorhabditis elegans* and that these life-span-extending capabilities of low-dose Li^+ can be observationally translated into reduced overall mortality in humans that have been exposed to comparable amounts of Li^+ in a similar long-term fashion [8]. The lithium ion Li^+ administered as any of several lithium salts has proved to be useful as a mood-stabilizing drug in the treatment of bipolar disorder due to neurological effects of the ion in the human body. Long-term treatment with lithium is associated with a preservation of memory function, increased hippocampal size in vivo, and increased gray matter [12]. A study by Al-Chalabi et al. investigated the role of Li_2CO_3 in amyotrophic lateral sclerosis patients and found that significant differences in the rate of functional deterioration measured by MRC Manual Muscle Testing scores (MMT; 18 % decline in Li_2CO_3+riluzole group versus 35 % in the riluzole only group). [13].

Recently, Helbich et al. [1, 14] found some interesting associations when they investigated the relation between suicide mortality, lithium levels in drinking water, and the altitude above sea level. These new research and methodological approaches contribute to the induction of new avenues in the collaboration between biology, chemistry, psychiatry, geographic information science, and even criminology, by exploring the association between lithium content in drinking water and mental health, and especially suicide mortality, as well as violent or impulsive crime [14–17].

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Conflict of Interest The authors do not have financial or nonfinancial competing interests by publishing this article.

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