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Research report

Trace lithium is inversely associated with male suicide after adjustment of climatic factors

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ABSTRACT

Background: Previously, we showed the inverse association between lithium in drinking water and male suicide in Kyushu Island. The narrow variation in meteorological factors of Kyushu Island and a considerable amount of evidence regarding the role of the factors on suicide provoked the necessities of adjusting the association by the wide variation in sunshine, temperature, rain fall, and snow fall.
Methods: To keep the wide variation in meteorological factors, we combined the data of Kyushu (the southernmost city is Itoman, 26°) and Hokkaido (the northernmost city is Wakkanai, 45°). Multiple regression analyses were used to predict suicide SMRs (total, male and female) by lithium levels in drinking water and meteorological factors.
Results: After adjustment of meteorological factors, lithium levels were significantly and inversely associated with male suicide SMRs, but not with total or female suicide SMRs, across the 153 cities of Hokkaido and Kyushu Islands. Moreover, annual total sunshine and annual mean temperature were significantly and inversely associated with male suicide SMRs whereas annual total rainfall was significantly and directly associated with male suicide SMRs.
Limitations: The limitations of the present study include the lack of data relevant to lithium levels in food and the proportion of the population who drank tap water and their consumption habits.
Conclusions: The present findings suggest that trace lithium is inversely associated with male but not female suicide after adjustment of meteorological factors.

1. Introduction

Several meta-analyses (Cipriani et al., 2005; Baldessarini et al., 2006; Cipriani et al., 2013) and randomized trials (Lauterbach et al., 2008; Oquendo et al., 2011) have shown anti-suicidal effects of lithium in people with mood disorders. Despite the fact that lithium levels in tap water are much lower than the so-called therapeutic levels, accumulating epidemiological studies investigate whether lithium may be effective for suicide attempt. An inverse association between lithium levels in drinking water and suicide rates was first reported in the USA from a sample of 27 Texas counties in 1990 (Schrauzer and Shrestha, 1990). Thereafter, we showed an inverse association between lithium levels in drinking water and suicide rates for 18 municipalities of Oita prefecture in Japan in 2009 (Ohgami et al., 2009). However, this association was not found in a sample derived from 47 subdivisions in the East of England (Kabacs et al., 2011) and the association remains uncertain in a sample derived from 145 sites in Italy where lithium concentrations and local suicide rates were not significantly inversely related, except in 1980–1989, particularly among women, and also, based on weighted least-squared, bivariate regression modeling, lithium concentrations were significantly and negatively associated with overall suicide rates (in women and men), but only in 1980–1989 (Pompili et al., 2015). A nationwide Austrian study found an inverse association between lithium levels in drinking water and suicide rates after adjustment of population density, per capita income, proportion of Roman

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Catholics, as well as the availability of mental health service providers (Kapusta et al., 2011). Furthermore, two recent studies, one conducted in Aomori prefecture of Japan (Sugawara et al., 2013) and the other in 34 province of Greece (Giotakos et al., 2013) also reconfirmed the inverse association between lithium levels in drinking water and suicide rates.

Moreover, in our most recent study (Ishii et al., 2015) investigating 274 municipalities of Kyushu Island in Japan, the associations of lithium levels in drinking water with suicide rates (total, male and female) were investigated adjusting for multiple variables such as proportion of elderly people, proportion of one-person households, proportion of people with college education or more, proportion of engaging in primary industry, overall unemployment rate, annual marriage rate, annual mean temperature and annual postal savings per person. As a result, lithium levels in drinking water were significantly and inversely associated with male suicide rates but not total or female suicide rates, suggesting that lithium in drinking water may be associated with the low risk of male suicide in the general population (Ishii et al., 2015).

Although we focused on Kyushu Island in the above study (Ishii et al., 2015), Japan has four large islands—Hokkaido, Honshu, Shikoku, and Kyushu. The northernmost island is Hokkaido whereas the southernmost island is Kyushu. The difference in latitude between Kyushu (the southernmost city is Itoman, 26°) and Hokkaido (the northernmost city is Wakkanai, 45°) is very large, suggesting considerable variations in climate (i.e. meteorological factors). There is a considerable amount of research concerning the role of meteorological factors on suicide such as the association of sunshine with suicide (Terao et al., 2002; Vyssoki et al., 2014), that of rainfall with suicide (Tsai, 2010; Tsai and Cho, 2012; Nicholls et al., 2006; Preti, 1998; Wu et al., 2014), and that of temperature with suicide (Tsai, 2010; Preti, 1998; Wu et al., 2014), thereby provoking the necessities of adjusting the association between lithium in drinking water and suicide ratios by meteorological factors.

In the present study, we investigated the association between lithium in drinking water and suicide rates of all 35 cities of Hokkaido Island and all 118 cities of Kyushu Island to adjust the association by the wide variation in sunshine, temperature, rain fall, and snow fall.

2. Methods

2.1. Suicide data

Taking the large differences in gender and age distribution of individual city populations into account, the standardized mortality ratio (SMR) of suicide in 2010 and 2011 was calculated for each individual city. We examined the data from Ministry of Health Labor and Welfare on suicide, and from Statistics Bureau, Ministry of Internal Affairs and Communications, and calculated total, male and female suicide SMRs for 2010 and 2011 across all 35 cities of Hokkaido Island and all 118 cities of Kyushu Island. We focused on the cities but not on the towns or villages in order to decrease heterogeneity of economic and cultural background as much as possible.

2.2. Measurement of lithium levels in drinking water

From 2010 to 2015, tap water samples (chiefly from the main rail station and/or the city office) of each city were taken and their lithium levels were measured by using mass spectroscopy analyzed by a third party. This method can measure very small amounts of lithium; the minimal amount of lithium that can be measured is 0.1 ppb (0.1 μg/l). If lithium levels of drinking water were measured at multiple points in the same city, the mean value was calculated. Although lithium levels were measured once in this study, we previously confirmed only a very small fluctuation in levels over time because the correlation coefficient between the lithium levels and those re-measured after 1 year in the same places was 0.998 (Ohgami et al., 2009). The distribution of lithium levels was also considerably skewed (skewness=4.3; kurtosis=24.0). We thus employed log-transformation (skewness=−0.01; kurtosis=0.26) in order to use parametric statistical procedures.

2.3. Meteorological factors

We initiated a crude model analysis of the association of lithium levels in drinking water and suicide SMRs (the average of suicide SMRs in 2010 and 2011 in total, male and female population) without any adjustment of the confounding factors (crude model). Furthermore, as previously mentioned, the associations were further investigated adjusting for meteorological factors such as annual total sunshine, annual mean temperature, annual total rainfall and annual total snowfall. Data from the Japan Meteorological Agency relating to these factors was available for two thirds of the 153 cities and was assumed to also represent the neighboring cities. Where meteorological data was unavailable for an individual city, the data from the neighboring city was extrapolated.

2.4. Statistical analysis

Due to differences in population size across the 153 cities, weighted least squares regression analysis adjusted for the size of each population was used to investigate the association of lithium levels in drinking water with the suicide SMRs as before (Ohgami et al., 2009; Ishii et al., 2015).

Multiple regression analyses were used to predict the average of suicide SMRs (total, male and female) in 2010 and 2011 by lithium levels in drinking water and meteorological factors (the average of annual total sunshine, annual mean temperature, annual total rainfall and annual total snowfall in 2010 and 2011). Multicollinearity was suspected if VIF value was above 10.

This study was approved by the ethics committee of Oita University Faculty of Medicine.

3. Results

3.1. Suicide rate, suicide SMR and lithium Levels

As for the average of suicide rate (2010 and 2011), 4039 deaths of 16981717.5 total population (23.8 per 100,000 population), 2871 deaths of 8040233.5 male population (35.7 per 100,000 population) and 1168 deaths of 8947561 female population (13.1 per 100,000 population) were identified in Kyushu and Hokkaido Islands. The average of mean total, male, and female suicide SMR (2010 and 2011) was 111.2 (SD 31.6; range 26.9–268.8), 119.1 (SD 38.6; range 0–245.0), and 97.1 (SD 44.9; range 0–319.0), respectively.

The mean lithium level in drinking water was 3.8 μg/l (SD 5.3; range 0.1–43) and the mean log-transformed lithium level in drinking water was 0.35 (SD 0.45; range −1 to 1.63). Annual mean