Declaration of interest

T.K. was a facilitator, R.B. a systematic reviewer and A.B. a guideline development group member for the NICE borderline personality disorder guideline.

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Lithium in drinking water

In their short report, Ohgami *et al*[1] reported lithium levels in drinking water and linked them to the risk of suicide. Despite the report highlighting the pitfalls of drawing simple conclusions from large-scale ecological studies, a Google search shows that these findings have been widely disseminated in scientific and lay media.

A major concern, addressed only obliquely by the authors, is the likelihood of confounding in this scenario. As noted by Chandra & Babu,[2] sociological factors play an important role in suicide.

The lack of accounting for such potential confounders for the different districts in the study is a serious methodological omission, rendering the results of the study untenable from an epidemiological perspective. The demographics of the different areas (beyond age structure) are not addressed, thus ignoring important economic and social factors (like deprivation and unemployment) which contribute to suicide risk.

Adjusting for differences in age structures between centres using standardised mortality ratios (SMRs) is unlikely to account for all important sources of confounding, so that the possibility of residual confounding must be considered a major qualifier when considering these results, rather than details to be addressed in future studies.[3]

The potential reasons behind the difference in lithium levels in the drinking water samples in the different municipalities are also not explained. Lithium levels in water sampled across a number of districts in New Zealand differ within municipal areas, depending where the sample is sourced. In this context, how valid is it then to use the mean value to represent the lithium exposure in that area? This would require the matching of lithium levels with suicide data from each discrete area of water supply and a loss of statistical power for such a relatively uncommon event as suicide.

The duration of exposure to a specific level of lithium in the drinking water was also not addressed. Apart from the issue of dietary intake of lithium noted in the letter by Desai & Chaturvedi,[4] there is the question of where people source most of their drinking water, and the use of bottled water.

In the context of the short report, it is also difficult to fully assess the suitability of the analysis methods used. It would have been useful to have more detail on the weighting structure used in the regression, alongside frequency data on the number of events observed in each locality. Also, the reported beta coefficient from the regression is not interpretable in the context of the presented figure or reported analysis methods.

Although the reported results were indeed intriguing, in the absence of more a developed approach to the research question it seems too early, and indeed misleading for a non-scientist audience, to even start speculating on the relationship between suicide rates and lithium in drinking water sources on the basis of these data. In this era of rapid information dissemination, the publishing of reports without rigorous scrutiny of the statistical method and due consideration of the confounding variables is a concern.

1 Ohgami H, Terao T, Shiotsuki I, Ishii N, Iwata N. Lithium levels in drinking water and risk of suicide. *Br J Psychiatry* 2009; **194**: 464–5.

2 Chandra PS, Babu GN. Lithium in drinking water and food, and risk of suicide. *Br J Psychiatry* 2009; **195**: 271.

3 Young AH. Invited commentary on . . . Lithium levels in drinking water and risk of suicide. *Br J Psychiatry* 2009; **194**: 466.

4 Desai G, Chaturvedi SK. Lithium in drinking water and food, and risk of suicide. *Br J Psychiatry* 2009; **195**: 271.

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In 1990 we reported that the mean suicide rates in 27 Texas counties over a 10-year period were consistently lower in those with 'high' natural lithium content in the drinking water (70–160 µg/l) than in counties with 'medium' (12–60 µg/l) or 'low' (0–10 µg/l) water lithium levels.[1] Ohgami *et al*[2] have since argued, without proof, that these associations may have been spurious owing to what they considered an arbitrary division of the data. It is necessary, therefore, to emphasise that the data were partitioned in accord with accepted methods of statistical trend analysis and not in an arbitrary fashion, and that tests were conducted to assure that the partitioning of the data did not produce spurious associations.

Within the same study,[1] we found the rates of homicide, rape, robbery, burglary and theft to be also lower in the high-lithium counties. In addition, a statistically significant reciprocal relationship between the water lithium levels and the arrest rates for possession of opium, cocaine and their derivatives was observed, while the arrest rates for lesser crimes such as possession of marijuana, drunkenness and driving under the influence showed no consistent dependence on the water lithium levels. The studies were later extended to include arrest rates of juveniles, yielding statistically significant results for possession of narcotic drugs and, interestingly, 'runaway from home'.[3]

In the interest of historical accuracy it needs to be pointed out that in 1972 Dawson *et al*[4] reported mental hospital admissions and homicide rates to be lower in high-lithium Texas counties. They also found the suicide rates to be lower in these counties, but the differences did not reach statistical significance, as incidence data for only a 2-year period (1968–1969) were compared.

Thus, the evidence in favour of beneficial effects of low levels of lithium on human behaviour is already strong, and since lithium is close to be officially recognised as a nutritionally essential trace element,[5] emphasis should be placed on assuring adequate lithium intakes in populations at risk of developing lithium deficiency.

1 Schrauzer GN, Shrestha KP. Lithium in drinking water and the incidence of crimes, suicides and arrests related to drug addictions. *Biol Trace Elem Res* 1990; **25**: 105–13.

2 Ohgami H, Terao T, Shiotsuki I, Ishii N, Iwata N. Lithium levels in drinking water and risk of suicide. *Br J Psychiatry* 2009; **194**: 464–5.

3 Schrauzer GN, Shrestha K. Lithium in drinking water and the incidence of crimes, suicides and arrests related to drug addictions. In *Lithium in Biology and Medicine* (eds GN Schrauzer, KF Klippel): 191–203. Verlag Chemie, 1991.

4 Dawson EB, Moore TD, McGanity WJ. Relationship of lithium metabolism to mental hospital admissions and homicide. *Dis Nerv Syst* 1972; **33**: 546–56.

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5 Schrauzer GN. Lithium: occurrence, dietary intakes, nutritional essentiality. *J Am Coll Nutr* 2002; **21**: 14–21.

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Authors' reply: First, Drs Huthwaite & Stanley point out that a major concern is the likelihood of confounding in this scenario. In our previous research,[1] we examined government statistics on suicide in the 47 prefectures in Japan. The overall yearly suicide rate in Japan was 25 per 100 000 population in 1999. Pearson's correlation was used to calculate correlations of suicide rate with latitude, longitude, yearly mean temperature, yearly total sunshine, yearly mean individual income, and yearly unemployment rate in the 47 prefectures, although lithium levels were not measured in the study. There was a significant correlation with suicide rate for yearly total sunshine, yearly mean temperature, latitude, and yearly mean individual income. By using multiple regression analysis, yearly total sunshine was the only individual variable to predict significant variance in suicide rate. Taking these findings into consideration, we did not use yearly mean individual income or yearly unemployment rate.[2] Also, yearly total sunshine was similar between the 18 municipalities of Oita prefecture so we did not use this. Most importantly, only 18 municipalities prevented us from conducting further analyses including confounding factors. We are now planning to perform a large study to consider confounding factors.

Second, they state that the potential reasons behind the difference in lithium levels in the drinking water samples in the different municipalities are also not explained and ask how valid it is then to use the mean value to represent the lithium exposure in that area. Lithium levels of drinking water supplies were measured at 26 locations in Oita city and at 53 locations in the other municipalities. The reason for the large difference in lithium levels is unknown, but Oita prefecture may have different geological features between the 18 municipalities and such differences may bring about large differences in lithium levels, although this thought is speculative. Also, instead of the mean value, we used the median value for the analysis and similar results were obtained.

Third, Huthwaite & Stanley question the duration of exposure to a specific level of lithium in the drinking water, and where people source most of their drinking water and the use of bottled water. In Japan, most people drink tap water although a small portion of people drink bottled water. Therefore, it is meaningful to measure lithium levels in tap water supplies. Moreover, the duration of exposure to a specific level of lithium is unknown, but if the residents continue to live at the same place, then their age may be associated with the duration.

Finally, we agree that in the context of the short report it is difficult to fully assess the suitability of the analysis methods used. Nonetheless, we emphasise that although short reports are not in themselves conclusive, they can provide new findings which lead to comprehensive research to establish a definite conclusion. We would like readers to read short reports with this in mind, so that they are not misled.

Although Schrauzer & Shrestha emphasise that their data were partitioned in accordance with accepted methods of statistical trend analysis, in their report[3] they said only that the 27 Texas counties were classified into high, medium, and low groups according to the lithium content in the municipal water supplies. There was no explanation of how to divide the high (range 70–160 μg/l), medium (13–60 μg/l) and low (0–12 μg/l) groups. To avoid the suspicion of an arbitrary division, they should have fully described their method in their full paper. In addition, their results were adjusted only by population density and annual income.

Dawson *et al*[4] also investigated suicide rates and lithium in drinking water, classifying lithium levels as high ($\geqslant$70 μg/l) or low ($\leqslant$11 μg/l). This division might have derived from their previous study, in which they reported that the lithium levels were clustered into four groups ($\leqslant$11, 11–29.9, 30.0–69.9 and $\geqslant$70 μg/l), which would provide about equal distribution of the measured values at consistent increments.[5] Their results were adjusted by population density, the distance to the nearest state hospitals and rainfall.[4]

Taking the nature of these partitions of lithium levels[3–5] into consideration, our method of investigating the association between suicide rates and lithium in drinking water[2] is more valid. We used lithium levels as a continuous variable and applied weighted least squares regression analysis adjusted for the size of each population. In any case, as Huthwaite & Stanley pointed out, confounding factors were not sufficiently investigated by Schrauzer & Shrestha[3], Dawson *et al*[4] or us.[2] Therefore, beneficial effects of low levels of lithium on human behaviour has not been confirmed and further studies are clearly required.

1 Terao T, Soeda S, Yoshimura R, Nakamura J, Iwata N. Effect of latitude on suicide rates in Japan. *Lancet* 2002; **360**: 1892.

2 Ohgami H, Terao T, Shiotsuki I, Ishii N, Iwata N. Lithium levels in drinking water and risk of suicide. *Br J Psychiatry* 2009; **194**: 464–5.

3 Schrauzer GN, Shrestha KP. Lithium in drinking water and the incidence of crimes, suicides and arrests related to drug addictions. *Biol Trace Elem Res* 1990; **25**: 105–13.

4 Dawson EB, Moore TD, McGanity WJ. Relationship of lithium metabolism to mental hospital admission and homicide. *Dis Nerv Syst* 1972; **33**: 546–56.

5 Dawson EB, Moore TD, McGanity WJ. The mathematical relationship of drinking water lithium and rainfall to mental hospital admission. *Dis Nerv Syst* 1970; **31**: 811–20.

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