Association between concentrations of chromium in drinking water and mortality due to suicide in Alabama

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ABSTRACT

Preclinical studies and clinical data from case series and placebo-controlled trials suggest that chromium might have antidepressant effects. We conducted an observational study in order to assess the association between concentrations of chromium in drinking water and mortality due to suicide in Alabama. Publicly available databases were used to determine both county-level concentrations of chromium in drinking water and county-level rates of mortality due to suicide in the years 2005–2015. Data analyses comparing county-level concentrations of total chromium in drinking water with mortality rate due to suicide were conducted using a two-tailed nonparametric Spearman's rank correlation, with statistical significance set at $p \leq 0.01$ and 99% confidence interval. Sub-analyses were conducted examining males, females, whites, and blacks/other minorities. There were no statistically significant findings concerning concentrations of chromium and suicide rate in the general population ($p = 0.35$, $r = -0.12$); however, there was a statistically significant inverse relationship between the concentration of chromium and suicide deaths in whites ($p = 0.009$, $r = -0.32$). There were no statistically significant findings in the remaining demographic subgroups. Chromium in drinking water might have a protective effect against mortality due to suicide, at least in the Caucasian population.

Key words | Alabama, chromium, drinking water, mortality, suicide

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HIGHLIGHTS

- Neuroprotective properties of chromium.
- Chromium levels in drinking waters.
- Potential ethnology based specific genetic component of chromium.
- Chromium's role in mental health.
- Association of chromium with rate of suicide.

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GRAPHICAL ABSTRACT

INTRODUCTION

Nearly 800,000 people die by suicide each year, which makes the phenomenon a significant public health issue (WHO 2020). In the United States, suicide is the tenth leading cause of death overall, but it is the second leading cause of death in age brackets encompassing 10–34 years old and the fourth leading cause of death in age brackets encompassing 35–54 years old. Even more concerning is the fact that age-adjusted suicide rates have continued to trend upwards every year since 2005 (NIMHS 2019). The majority of those who die by suicide have a mood disorder, such as major depressive disorder (USHHS 2014).

Essential elements are required for the proper functioning of the human body, and deficiencies of essential elements can cause various health risks (Młyniec *et al.* 2014). For example, many elements have an effect on neurotransmission, and there is evidence to suggest that deficiencies of essential elements might be involved in the pathophysiology of psychiatric disorders, such as depression (Młyniec *et al.* 2014). One such essential element is chromium. Various preclinical studies using rats have suggested that chromium picolinate and chromium chloride possess antidepressant properties owing to effects on monoaminergic (e.g., serotonergic) and glutamatergic systems (Młyniec *et al.* 2014). Clinical case series and clinical trials reported to date have mostly bolstered the hypothesis that chromium supplementation could have therapeutic benefits in the treatment of depression. Two initial case series reports described the successful use of chromium in depression – one that involved chromium picolinate augmentation (200–400 mcg/day) of antidepressant therapy in five patients with refractory dysthymic disorder, and one that involved chromium monotherapy either as picolinate or polynicotinate (400–600 mcg/day) in eight patients with refractory mood disorders (McLeod *et al.* 1999; McLeod & Golden 2000). Davidson *et al.* conducted a double-blind, placebo-controlled, randomized trial of chromium picolinate 600 mcg/day in 15 patients with atypical depression. The results revealed statistically significant improvement with chromium versus placebo on both response rate (70% versus 0%; $p = 0.02$) and remission rate (60% versus 0%; $p = 0.04$), although chromium did not show significantly greater benefit than placebo on the final Hamilton Depression Rating Scale (HAM-D) score (Davidson *et al.* 2003). Docherty *et al.* conducted a double-blind, placebo-controlled trial of chromium picolinate 600 mcg/day in

113 outpatients with atypical depression. Although the results did not show a significant difference between chromium and placebo on the primary outcome measures (i.e., HAM-D and Clinical Global Impression [CGI]-Improvement), the chromium-treated group experienced significant improvements compared with the placebo-treated group on the HAM-D items of appetite increase, increased eating, carbohydrate craving, and diurnal variation of feelings. Moreover, in a subpopulation of patients with high carbohydrate craving, chromium-treated patients had a significantly greater response rate on total HAM-D scores compared with placebo-treated patients (65% versus 33%; $p < 0.05$) (Docherty *et al.* 2005). Finally, Brownley *et al.* (2013) conducted a small double-blind, crossover study of chromium polynicotinate 400 mcg/day or placebo augmentation of sertraline 50 mg/day for the treatment of premenstrual dysphoric disorder. Four of the five study participants who showed marked improvement in HAM-D and CGI-Severity scores during sertraline treatment experienced greater changes in these outcome measures during treatment with chromium versus during treatment with placebo (Brownley *et al.* 2013).

Thus, whereas more definitive studies are needed to demonstrate that chromium is effective as monotherapy and/or adjunctive therapy in the treatment of depression, current data are rather encouraging in this regard. Many questions remain, but one rather intriguing question is whether chromium might have an antisuicidal effect. Lithium – another essential element – has antidepressant effects and has unequivocal evidence that it has a suicide prevention effect (Lewitzka *et al.* 2015). Interestingly, many studies have found that lithium in drinking water is associated with reduced risk of suicide in the general population in a dose-dependent manner (Vita *et al.* 2015; Barjasteh-Askari *et al.* 2020). Since chromium is present in natural waters in the environment at 2 ppb or less (Environmental Protection Agency (EPA) maximum level of 100 ppb) (USEPA 2017), it is possible that exposure to chromium via this source might also affect suicide risk in a dose-dependent manner. The objective of the current study was to assess the association between concentrations of chromium in drinking water and mortality due to suicide in the state of Alabama. Moreover, we sought to consider gender and race as associative variables.

METHODS

Water boards were identified using the Safe Drinking Water Information System (SDWIS), a national database of water suppliers published by the EPA (USEPA 2019). The SDWIS was used to find the number of water suppliers in each county of Alabama, their primary water source, and the population served by each. This information was used to calculate population weights for each water company supplying a level during the same sampling period. Data regarding concentrations of chromium in drinking water were collected from Consumer Confidence Reports (CCRs) – reports published on a yearly basis by individual water companies – either via the water company's website or from the Environmental Working Group or New York Times databases (NYT 2012; EWG 2020). 'Not detected' levels were substituted for the method detection limits for aqueous ion scanning mode values divided by 10 as listed in Table 7 of chapter 200.8 of the EPA's Methods for mass spectrometry (USEPA 1994). Water quality data for chromium from each supplier were multiplied by population weight to determine an average chromium level for the entire county. The aggregate levels per county were then averaged across the years 2005–2015.

Data regarding annual rates of mortality due to suicide were obtained from the Alabama Department of Public Health (ADPH), which releases its County Health Profiles every year (ADPH 2019). This database includes the average rate of suicide per 100,000 population in each county of Alabama, and it further divides the data into male, female, white, and black/other minorities. Mortality due to suicide per county were averaged over the years 2005–2015.

Data analyses comparing county-level concentrations of chromium in drinking water with mortality rate due to suicide were conducted using a two-tailed nonparametric Spearman's rank correlation (GraphPad Prism version 6.07), with statistical significance set at $p \leq 0.05$ and 95% confidence interval. Correlation coefficients (*r*-values) were determined from plots of chromium versus mean suicide rate normalized to a population of 100,000 using linear regression (GraphPad Prism version 6.07). Sub-analyses were conducted examining males, females, whites, and blacks/other minorities.

This research project was exempt from Institutional Review Board approval. We utilized publicly available data, and there were no human research subjects.

RESULTS

Table 1 shows chromium concentrations in drinking water and mortality rates due to suicide in all 67 counties of the state. The mean concentration of chromium across all counties was 0.0828 ± 0.1885 ppb. Sixteen counties had essentially undetectable chromium concentrations, whereas ten counties had concentrations of at least 0.1 ppb, with the highest chromium concentration exceeding 1.2 ppb. The mean suicide rate across all counties was 13.90 ± 3.99 per 100,000 from 2005 to 2015. The mean suicide rate across all counties for males, females, whites, and blacks/other minorities were 23.11, 5.14, 18.52, and 4.16 per 100,000, respectively.

Table 2 shows results from the analyses of the associations between chromium concentrations in drinking water and rates of mortality due to suicide. There were no statistically significant findings concerning concentrations of chromium and suicide rate in the general population; however, there was a statistically significant inverse relationship between the concentration of chromium and suicide deaths in whites ($p = 0.01$, $r = -0.32$). There were no statistically significant findings in the remaining demographic subgroups.

DISCUSSION

To our knowledge, this was the first observational study that has examined the possible antisuicidal effects of chromium in the general population. We found that chromium concentrations in drinking water were significantly inversely related with suicide rates in Caucasians, with the strength of the association being moderate. There were no such significant findings in the general population or in blacks/other minorities, and we cannot explain why this apparent protective effect of chromium was limited to Caucasians. Placebo-controlled studies of chromium in depression offer no assistance in the regard. Race of participants was not delineated by Brownley *et al.* (2013), all but one patient in the study by Davidson *et al.* (2003) were Caucasian, and 81% of the evaluable population in the study by Docherty *et al.* (2005) were Caucasian, with no sub-analysis of results by race offered by the researchers. However, there could potentially be an ethnology based specific genetic component which supports further detailed and focused investigations of our findings.

The mean concentration of chromium in drinking water in this study (i.e., 0.08 ppb, which equates to 0.08 mcg/L) was remarkably low, and it was well below the federal drinking water standard for total chromium of 100 ppb (USEPA 2017). Given that clinical trials examining chromium for the treatment of depression have used doses of 400–600 mcg/day, it is tempting to discount the possible therapeutic effects of a mere fraction of that amount that can be consumed through water intake. However, the situation might be analogous to what is seen with lithium, which is found in drinking water at considerably lower amounts than are used in clinical practice. Medicinal doses of lithium carbonate are on the order 600–2,400 mg/day, but epidemiological studies that have found negative correlations between lithium levels and suicide rates have maximum lithium concentrations that are usually <200 mcg/L (Szklarska & Rzymski 2019). Thus, it could be that chronic exposure to even relatively minor amounts of trace elements in drinking water can achieve therapeutic effects, and furthermore, that differential effects can be seen with exposure to trace elements even within a relatively narrow concentration range.

Chromium is present in drinking water in both trivalent (chromium-3) and hexavalent (chromium-6) forms. Chromium-3 is the biologically active, essential dietary element, whereas chromium-6 is the toxic form that results from natural erosion of chromium deposits and from industrial pollution (USEPA 2017; NIHODS 2019). Water systems are required to test for total chromium, which includes both chromium-3 and chromium-6, because the two forms can convert back and forth in water (USEPA 2017). With chronic exposure, chromium-6 can cause adverse dermatological effects, such as allergic dermatitis, which is the basis for the federal drinking water standard noted above (USEPA 2017). Concerns have been raised about the possible carcinogenic effects of chromium compounds with long-term use

Table 1 | Chromium concentrations in drinking water and suicide rates in all counties of Alabama (2005–2015)

		Mean suicide rate (per 100,000)				
County	**Mean chromium level (ppb)**	**General population**	**Males**	**Females**	**Whites**	**Blacks/other**
Autauga	0.0139	16.03	25.60	6.97	17.96	8.68
Baldwin	0.0734	18.07	28.59	8.00	19.99	4.95
Barbour	0.1114	9.90	14.89	4.22	15.64	3.94
Bibb	0.0008	16.46	25.69	6.11	20.47	3.50
Blount	0.2066	16.63	25.88	7.53	17.18	4.02
Bullock	0.6006	8.43	12.33	3.77	15.58	5.82
Butler	0.0008	11.13	19.06	4.15	19.50	0.96
Calhoun	0.0698	15.77	28.55	3.95	18.70	6.13
Chambers	0.0144	11.67	20.55	3.56	16.57	4.61
Cherokee	0.4631	21.15	37.07	5.69	22.36	5.55
Chilton	0.0015	16.81	27.26	6.64	18.58	5.11
Choctaw	0.0008	9.92	19.42	1.29	14.20	4.46
Clarke	0.0008	10.92	18.58	4.03	17.37	3.12
Clay	0.0008	13.34	25.73	1.28	16.11	0.00
Cleburne	0.4384	19.05	32.02	6.07	20.15	0.00
Coffee	0.0522	13.04	22.71	3.65	16.55	1.53
Colbert	0.0827	14.67	25.32	4.80	17.65	1.75
Conecuh	0.0008	20.20	33.54	8.09	35.42	3.03
Coosa	0.0008	25.02	43.44	6.63	34.80	5.09
Covington	0.3104	13.39	23.28	4.21	14.30	8.05
Crenshaw	0.0210	15.05	17.65	12.55	19.81	2.45
Cullman	0.0493	16.83	27.46	6.43	17.47	0.00
Dale	0.0063	13.30	21.42	5.45	16.77	2.97
Dallas	0.0196	8.50	15.71	2.38	18.80	3.99
DeKalb	0.1626	14.28	21.05	7.69	15.26	2.85
Elmore	0.0023	13.89	21.13	6.74	16.71	4.90
Escambia	0.0423	10.35	19.26	0.98	14.54	3.22
Etowah	0.0376	14.47	24.00	5.60	16.25	6.62
Fayette	0.0008	18.95	34.31	4.07	21.27	3.88
Franklin	0.0443	14.81	23.89	5.80	15.81	4.75
Geneva	0.0008	17.65	31.15	4.71	18.65	10.76
Greene	0.0008	10.09	15.07	5.97	32.12	4.93
Hale	0.0008	9.11	16.32	2.13	17.06	3.61
Henry	0.0008	18.25	30.24	7.21	25.68	1.76
Houston	0.0283	12.65	21.24	4.80	15.66	5.25
Jackson	0.0082	18.33	32.15	5.02	19.78	2.12
Jefferson	0.0438	12.75	21.68	4.75	18.35	5.95
Lamar	0.5014	12.01	18.28	6.08	13.05	4.99

(*continued*)

Table 1 | continued

		Mean suicide rate (per 100,000)				
County	**Mean chromium level (ppb)**	**General population**	**Males**	**Females**	**Whites**	**Blacks/other**
Lauderdale	0.0134	12.20	20.05	4.99	13.58	2.25
Lawrence	0.0033	20.55	36.06	5.74	25.14	3.72
Lee	0.0085	9.58	14.66	4.58	11.82	3.73
Limestone	0.0016	12.01	18.73	5.13	13.35	5.36
Lowndes	0.1307	5.65	10.50	1.31	11.54	3.42
Macon	0.0008	9.10	18.01	1.52	24.39	6.16
Madison	0.0465	13.25	21.28	5.56	17.10	4.15
Marengo	0.0672	8.35	12.30	4.99	13.03	4.17
Marion	0.0469	18.43	26.23	10.79	19.26	5.62
Marshall	0.0348	14.67	25.08	4.86	15.22	6.97
Mobile	0.0017	13.62	22.73	5.24	18.26	6.35
Monroe	0.0543	13.35	21.16	6.19	19.60	5.46
Montgomery	1.2453	9.81	16.31	3.90	16.76	4.85
Morgan	0.0100	16.15	25.38	7.16	18.45	3.85
Perry	0.0224	6.89	9.23	4.78	16.81	2.47
Pickens	0.0333	11.12	18.42	4.35	15.50	5.29
Pike	0.0008	17.21	28.40	7.01	23.65	7.81
Randolph	0.0169	18.45	36.47	1.55	23.36	1.72
Russell	0.0261	15.27	24.73	6.55	24.27	4.48
Shelby	0.0923	13.61	21.56	5.96	15.52	2.59
St. Clair	0.0888	17.28	28.65	5.84	19.00	3.83
Sumter	0.0339	5.39	8.96	2.44	16.14	1.85
Talladega	0.0339	14.48	24.67	4.84	19.21	5.26
Tallapoosa	0.0008	11.95	19.21	5.14	14.86	4.70
Tuscaloosa	0.0010	11.03	18.38	4.15	14.80	3.46
Walker	0.0008	20.91	36.13	6.55	22.19	6.63
Washington	0.0120	15.38	23.83	7.29	20.97	4.53
Wilcox	0.0864	7.44	12.91	2.66	19.24	2.95
Winston	0.0166	15.40	26.72	4.45	15.90	0.00

ppb, parts per billion.

of chromium nutritional supplements (Levina & Lay 2008; Wu *et al.* 2016); however, exposure to chromium levels in drinking water has been deemed to be of low/no concern for public health (EFSA 2014).

The suicide rates in this study were reasonably consistent with expected values. For example, the mean suicide rate across all counties in Alabama from 2005 to 2015 was 13.90 per 100,000 compared with the national average of 12.04 per 100,000 over the same time period (NIMHS 2019). The suicide rate was approximately 4.5 times higher among males versus females and among whites versus blacks/other minorities, whereas national data reveal that the suicide rate among males is approximately 4 times higher than among females and the suicide rate among white non-Hispanics is approximately 3 times higher than among black non-Hispanics (NIMHS 2019).

Table 2 | Associations between chromium concentrations in drinking water and suicide rates

Demographic group	p-value	r-value
General population	0.35	−0.12
Male	0.22	−0.15
Female	1.00	< 0.01
White	0.01*	−0.32
Black/other	0.93	0.01

*Statistically significant.

This investigation utilized large amounts of publicly available data from official sources. Annual data were collected over the range of many years in order to avoid potential aberrant values. On the other hand, there were several limitations to this investigation. First, water quality data were sometimes difficult to obtain and/or interpret, so there were some voids in data collection. Next, the study relied on chromium concentrations in drinking water, which may or may not reflect actual intake of chromium. Similarly, chromium can be consumed via other sources besides drinking water, such as vegetables, fruits, meats, vitamin supplements, and grains (USEPA 2017; NIHODS 2019), but there was no way to assess such intake or determine its impact on the result. The study examined suicide rates and chromium concentrations in water within particular counties, so there was an assumption of static geographic locations of populations. Finally, the suicide rates were acquired from publically available websites and may not account for unreported or misreported incidents. Of course, these are all typical examples of limitations of epidemiological observational studies.

CONCLUSION

Chromium in drinking water might have a protective effect against mortality due to suicide, at least in the Caucasian population. These preliminary findings justify continued and detailed investigations in Alabaman as well as in different geographic locations to support the reported finding, with a particular emphasis on the possible role of race as a contributing factor.

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

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