Lithium supplements to prevent Alzheimer’s disease: A poisoned chalice?

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Matthew J. Armstrong, Anthony E. Valenzuela, and Pamela J. Lein explore the use of lithium supplements to prevent Alzheimer’s disease and whether this approach is a poisoned chalice

Globally, an estimated 55 million people live with Alzheimer’s disease, a number expected to exceed 152 million by 2050. Alzheimer’s is a progressive and fatal neurodegenerative disease and the most common form of dementia. There are no cures for Alzheimer’s, and currently available treatments only modestly slow disease progression. Identifying effective therapeutics has been difficult because while genetic factors contribute to Alzheimer’s, cases with single causative mutations are rare (1-5%).

Rather, most cases of Alzheimer’s are caused by complex interactions between any number of genetic susceptibilities and environmental factors, like lifestyle and exposure to pollutants. Because variable genetic and environmental contributions determine individual risk and severity of Alzheimer’s, it may be more appropriate to consider Alzheimer’s as a group of diseases (akin to cancer) in which many types exist, and treatments may be effective in one individual but not another.

Lithium supplements to prevent Alzheimer’s disease

A recent study published by Dr. Liviu Aron and Dr. Bruce Yanker at Harvard Medical School in the journal Nature identified lithium (Li) as a potential treatment for decreasing the time to onset and/or slowing the progression of Alzheimer’s in a mouse model. This report has generated significant interest via online forums, with the findings translated into numerous reports more accessible to laypersons. However, many of the nuances articulated in the original article regarding lithium toxicity have been lost in translation. Given the desperation of many Alzheimer’s patients and their loved ones to find a cure, the easy accessibility to lithium as an over-the- counter supplement has raised significant public health concerns.

While physicians have used various lithium formulations (e.g., lithium carbonate) since the 1800s to treat diverse neurological and psychiatric disorders, such as epilepsy, bipolar disorder, schizophrenia, and depression, how lithium works to alleviate symptoms of neurological disease is not well understood. In addition, there are serious toxic risks associated with lithium, including adverse neurological, renal, cardiovascular, gastrointestinal, and endocrine effects, as well as an increased risk of cardiac birth defects if taken during pregnancy. Most notably, approximately 50% of individuals regularly taking lithium develop nephrogenic diabetes insipidus, a potentially serious reduction in the kidney’s ability to concentrate urine that can lead to rapid and severe dehydration. Left untreated, lithium toxicity can be fatal.

When a doctor prescribes lithium, regular blood tests are performed to carefully monitor the blood concentration of Li to prevent toxicity. However, lithium toxicity can occur even with careful medical monitoring.

This is because there is a narrow margin between a safe therapeutic dose and a toxic dose. A 25% increase in dose significantly increases the risk of toxicity; a greater than 67% increase can be life-threatening.

Lithium toxicity risk factors and research

Several factors can modulate the risk of lithium toxicity. For example, the body handles lithium similarly to sodium, which it resembles on a molecular level. Conditions that cause a loss of sodium and water from the body, such as vomiting, diarrhea, fever, or excessive sweating, can significantly increase lithium reabsorption in the kidneys, thereby increasing the risk of adverse effects.

Drug interactions between lithium and prescription or over-the-counter drugs are also a serious concern. Nonsteroidal anti-inflammatory drugs, like ibuprofen, naproxen, and aspirin, interact with lithium supplements to elevate lithium levels in the blood. This is also the case for several common drugs that affect kidney function, such as some blood pressure medications (ACE inhibitors and angiotensin II receptor blockers) and diuretics.

Lithium can also affect how other medications work in the body, increasing the risk of adverse effects. For example, combining lithium with antidepressants that increase serotonin in the brain, like selective serotonin reuptake inhibitors (SSRIs) and monoamine oxidase inhibitors (MAOIs), increases the risk of serotonin syndrome. In this condition, serotonin is elevated to life-threatening levels.

To reduce the risk of toxicity associated with lithium, researchers have begun investigating different chemical forms of lithium, including lithium orotate (LiO), that potentially provide improved therapeutic effectiveness at lower doses. While doctors have prescribed lithium carbonate and citrate for decades, LiO is not FDA-approved and cannot be prescribed by physicians; however, it is readily available for purchase over the counter. Currently, only one pre-clinical safety assessment on LiO is available, and there are no clinical safety assessments.

While early research on LiO appears promising, we are far from understanding the benefits and risks of its use as a treatment for Alzheimer’s. The potential dangers of unsupervised lithium supplementation are compounded by the lack of FDA regulation of lithium supplements. Supplements are not rigorously tested for safety pre-market, nor are they approved to prevent, treat, or cure disease. In addition, multiple studies have found that dietary supplements on the market often have much higher or lower doses than advertised, unlisted ingredients, or hazardous heavy-metal contaminants, such as lead.

Does lithium show promise as a potential therapeutic for Alzheimer's?

Although lithium shows promise as a potential therapeutic for Alzheimer's in preliminary studies, significant questions remain regarding its efficacy and safety in humans. While neuroprotective effects were observed in mouse models, the models used in the Harvard study represented a rare (1-5% of cases) form of AD; thus, it remains to be determined whether the results generalize to humans or to the other ~95-99% of human cases.

Finally, the long-term safety of LiO has not been established through human studies; moreover, dietary LiO supplements are minimally regulated compared to FDA-approved medications, which must meet safety, purity, and dose-testing standards. The ready availability of LiO as over-the-counter supplements enables consumers to self-administer without medical supervision, dose monitoring, or screening for drug interactions. These dangers outweigh the unknown benefits lithium may have on AD pathology in humans.

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