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Five Supplements and Multiple Psychotic Symptoms:

A Case Report

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ABSTRACT

Dietary supplements, including vitamins, minerals, herbs, amino acids, and enzymes, have become increasingly more common and are used by approximately half of the US population. About three-fourths of supplements are obtained with no prescription from a physician, which raises medical concerns regarding safety as these products do not require US Food and Drug Administration approval. Common reasons for taking dietary supplements include improved mood, improved mental function, depression relief, anxiety reduction, and treatment of simple and migraine headaches. The use of herbs for medicinal purposes has a long-standing history among many cultures. We present the case of a 43-year-old man, who was taking dietary supplements, with a 6-month history of psychotic symptoms that increasingly caused impairment in functioning and eventually led to involuntary hospitalization. The published data with regard to supplements causing psychosis, herb-to-herb interaction, and reliability of herbal supplement manufacturers are discussed.

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Dietary supplements, including vitamins, minerals, herbs, amino acids, and enzymes, have become increasingly more common and are used by approximately half of the US population.¹ About three-fourths of supplements are obtained with no prescription from a physician,¹ which raises medical concerns regarding safety as these products do not require US Food and Drug Administration approval. Common reasons for taking dietary supplements include improved mood, improved mental function, depression relief, anxiety reduction, and treatment of simple and migraine headaches. According to a recent study² that examined over 2,000 subjects per year from 2007 to 2011, supplement use increased over that time period. The primary reasons given for supplement use are overall health and filling nutrition gaps.² However, it is impossible to make any generalizations about the usefulness of such remedies, especially as the data generally are lacking risk-benefit profiles.³

Several research studies have correlated the use of certain herbs and supplements to various psychiatric problems. In a study⁴ of 63 patients with psychiatric disorders in the emergency department, 15.9% (n = 10) reported regular supplement use. One patient who was taking risperidone was using kava,⁴ which has been shown to increase the hallucinogenic effects of psychoactive agents.^{5,6} In a case report,⁷ a potential relationship was found between the use of horny goat weed, an herb used to treat erectile dysfunction, and the development of hypomania. In another case,⁸ ginkgo biloba, an herb used for memory enhancement and blood flow improvement, was linked to the presentation of hypomania when taken in conjunction with St John's wort, fluoxetine, and melatonin. The increasing popularity of dietary supplements necessitates further investigation into the effects of supplement use in the psychiatric patient population.

We present the case of a 43-year-old man who was taking dietary supplements and had a 6-month history of psychotic symptoms that increasingly caused impairment in functioning, eventually leading to involuntary hospitalization. The published data with regard to supplements causing psychosis, herb-to-herb interaction, and reliability of herbal supplement manufacturers are discussed. We individually searched PubMed and collaborated on relevant literature findings. Publications were selected after considering the quality of connections made between supplements used by the patient in our case report and psychosis. Various keywords were used in the PubMed searches including “supplements and psychosis” and “dopamine and herbs.” No language or date restrictions were used in the search. Additional sources were drawn from the reference lists of key publications.

CASE REPORT

Mr A, a 43-year-old white man with no prior psychiatric history, was admitted as an inpatient to the University of California, Irvine, medical psychiatric unit after exhibiting concerning behaviors accompanied by a 6-month history of auditory and visual hallucinations. He reported hearing voices telling him to leave his workplace or his family when they were outside of the home. On several occasions, he acted on the hallucinations. Once he left his family at the park without telling them, drove to random locations, and did not answer his phone. His family had to arrange another mode of transportation home. He also was seeing random faces and started having violent visions of hurting himself with a knife. Mr A described

- With the growing herbal supplement industry, more patients are presenting with supplement-associated toxicities.
- The limited research available on supplement toxicities is a barrier to clearly diagnosing supplement-induced psychosis.
- Primary care physicians can make a difference by educating their patients on supplement use.

having paranoid thoughts that someone was listening to his phone calls and reading his e-mails at work: he believed that someone else was responsible for his car's flat tire and his father's car accident. His sleep and appetite also had decreased during this time. Mr A failed to fulfill criteria for depression. He endorsed hopelessness but no anhedonia or depressed mood. He denied symptoms of mania and had no past psychiatric history, no past medical history, no medications, and no family history of psychiatric illness. He denied tobacco or recreational drug use and was drinking 1 beer per week. Physical and cognitive examinations were normal. His vital signs, complete blood count, electrolytes, drug screen, and urinalysis were unremarkable aside from a vitamin B₁₂ level on the lower end of normal (240 pg/mL; normal: 180–1,241 pg/mL). A noncontrast computed tomography scan showed no acute intracranial abnormalities; no evidence of intracranial mass, hemorrhage, or midline shift; and normal ventricles, sulci, and cisternal spaces. At admission, he was calm and cooperative with a linear thought process.

A pertinent finding from the history and medical workup was that Mr A had started 5 dietary supplements (Table 1): *Garcinia cambogia*, Brain Support, Brain Awake, a probiotic, and Absorbmax, which was taken to lose weight and sharpen his mind when the hallucinations began. After admission, he was started on risperidone titrated to 2 mg for psychosis, diphenhydramine 25 mg twice/day for sleep and restlessness, and cyanocobalamin 1,000 mcg oral tablet for supplementation. His hallucinations improved on this regimen. Mr A was told to discontinue all supplement use. He continued to show constricted affect but was calm throughout his hospitalization and participated in therapy groups and slept and ate well. After 4 days of inpatient care, his psychosis decreased significantly, and he was discharged to a partial hospitalization program where his symptoms continued to improve. After completing the partial program, he returned to work and followed up with a psychiatrist and therapy. At the first outpatient visit, he reported that the auditory hallucinations were “mostly gone” and the volume was “turned down.” However, he reports that he does not feel as productive at home and work compared to before starting the supplements. He also expressed concern that, despite significant improvement, he will not return to his previous level of functioning. Risperidone was increased to 1 mg in the morning and 3 mg at bedtime. At a follow-up visit, his episodes of psychosis were completely resolved, and risperidone was decreased with a plan to taper him off the drug entirely.

Table 1. Ingredients in the 5 Supplements Taken by Mr A

<i>Garcinia cambogia</i> (various manufacturers)
Chromium
<i>Garcinia cambogia</i> (hydroxycitric acid)
Green coffee bean extract (<i>Coffea canephora robusta</i>)
Raspberry ketones
Brain Support (Irwin Organics)
Ginkgo powder
Blueberry powder (<i>Vaccinium angustifolium</i>)
Asian ginseng powder
Grape powder
Ginger powder
Papaya powder
Brain Awake (Irwin Organics)
Vitamin B ₆ (pyridoxine hydrochloride)
Folate
Vitamin B ₁₂
MCT (medium chain triglyceride) oil
Acetyl-L-carnitine
Bacopa extract
Holy basil (<i>Tulsi</i>) extract (2% ursolic acid)
Alphawave L-theanine
InnovaTea natural tea extract
Lemon balm extract
Rosemary extract (3% rosmarinic acid)
Bioperine black pepper
Ginger extract
Other ingredients: flaxseed oil, gelatin, purified water, glycerin, beeswax, soy lecithin, St John's bread, silicon dioxide, and titanium dioxide
Probiotic (various manufacturers)
<i>Lactobacillus acidophilus</i>
<i>Lactobacillus paracasei</i>
<i>Bifidobacterium lactis</i>
<i>Bifidobacterium bifidum</i>
<i>Lactobacillus plantarum</i>
<i>Lactobacillus rhamnosus</i>
Absorbmax (BioTRUST Nutrition)
Protease SP
Protease S
Aspergillopepsin
Peptidase
Amylase
Glucoamylase
Lipase
Lactase
α-Galactosidase
Phytase
Cellulase
β-Glucanase
Hemicellulase
Pectinase
Xylanase
Bromelain
Cayenne pepper
Trace minerals
Ginger rhizome

LITERATURE REVIEW

There is an increasing repertoire of reports⁹ detailing various psychiatric and neurologic effects related to the consumption of herbal medicines. Although the etiology is unclear, in the absence of other confounding factors, we suggest that Mr A's acute-onset psychosis was caused by herbal supplementation.

Supplements and Psychosis

Interestingly, few case reports have demonstrated a link between herbal supplements found in Mr A's supplement

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regimen and the onset of severe psychiatric conditions in patients with no prior psychiatric histories. Evcimen et al¹⁰ reported that acetyl-L-carnitine, an ingredient listed in Brain Awake, was temporally indicated in the onset of psychosis in a male patient who presented with auditory hallucinations. Furthermore, Norelli and Xu¹¹ reported *Panax ginseng*-induced mania in 2 patients who were consuming ginseng on a daily basis and whose symptoms rapidly remitted after discontinuation of the supplement.

Herb-Herb Interactions

Mr A's simultaneous use of 5 different dietary supplements was pertinent in his case, as interactions between multiple herbs have been found to cause psychiatric symptoms. Ginger rhizome, present in 3 of Mr A's supplements, was part of a 5-ingredient Chinese supplement found to have antidepressant-like effects through mediating serotonergic and dopaminergic reuptake.¹² Another study¹³ on herbal extracts included grape seed, green tea, and ginkgo, ingredients in Brain Awake and Brain Support. These and several other herbs were found to inhibit sulfotransferase 1A3, a phase II detoxifying enzyme in the intestinal epithelium that modulates dopamine sulfation, thus increasing the bioavailability of dopaminergic drugs.¹³ With the effect of elevated dopamine levels in psychosis, the ability of these herbal interactions to modulate dopamine metabolism and reuptake may have contributed to Mr A's psychotic symptoms.

Reliability of Herbal Supplement Manufacturers

The reliability of effects from herbal supplements is further confounded by investigating the regulation of these over-the-counter medications. According to the National Center for Complementary and Integrative Health,¹⁴ herbal supplement manufacturers may not know or list all of their ingredients. Contaminated herbal supplements have been linked to cerebral edema, coma, confusion, central nervous system depression, encephalopathy, vocal tics, movement disorders, muscular problems, paresthesia, and seizures.⁹ Irwin Naturals, the company that manufactures Brain Support and Brain Awake, was charged with false and misleading advertisements, failing to adequately relay the lead content of its products, and selling Hoodia supplements that did not in fact contain any of the stated active ingredient, *Hoodia gordonii* herb.¹⁵

CONCLUSION

With the wide use of dietary supplements, it is becoming increasingly important for physicians to expand their

knowledge to recognize the toxicities of supplement ingredients and the potential herb-herb interactions in patients taking multiple supplements. In addition, the lack of a reliable regulatory body to monitor the herbal supplement industry shifts more responsibility to the physician to engage and educate patients about their choices in consuming these products. When a patient presents with acute psychiatric symptoms, recent supplement use, and a seemingly negative history, physical examination, and test workup, identifying the effects of supplement usage may prove useful in directing clinical decision-making.

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