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Case Report

Mania following addition of hydroxytryptophan to monoamine oxidase inhibitor

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Abstract

This case report highlights the risk of nutritional supplements and misinformation obtained from the internet particularly for those on monamine oxdiase inhibitors (MAOIs). Despite sophisticated medical knowledge, this patient, who was taking an MOAI and complying with a tyramine-free diet, used a supplement of hydroxytryptophan that along with the MAOI appears to have precipitated mania, despite no personal or familial history of bipolar disorder.
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Keywords: Monamine oxidase inhibitor (MAOI); Hydroxytryptophan; Mania; Internet; Serotonin syndrome

1. Introduction

Over-the-counter (OTC) medications/supplements place patients at risk for drug interactions. For example, almost one third of adults aged 57 through 85 years took at least five prescription medications; among prescription medication users, 46% took OTC medications and 52% took nutritional supplements — placing 4% at risk for major drug–drug interactions [1]. Monoamine oxidase inhibitors (MAOIs) can produce serious interactions. Fear of these prevents judicious use, particularly since MAOIs can frequently offer relief in treatment-resistant major depression disorder (TRD; MDD) [2]. This case shows the likely potential to precipitate mania by addition of L-hydroxytryptophan (5-HTP) to an antidepressant regimen including an MAOI. It highlights the ongoing need to caution patients taking MAOIs, even if sophisticated in biomedical knowledge, about taking adjuvant OTC drugs and nutritional supplements.

2. Case

This 60-year-old engineer, whose son had committed suicide, had TRD and restless legs syndrome. Neither he nor any family member had a history of mania. He had numerous past psychiatric hospitalizations for MDD and was treated with a myriad of modalities often used for TRD. He had steroid-dependent asthma treated with the usual medications and with intermittent brief pulses of prednisone during acute exacerbations.

Two years before this presentation, he developed acute respiratory distress syndrome requiring many weeks in the intensive care unit. Because he relapsed subsequently into a prolonged major depressive episode, phenelzine (MAOI) was selected. He had not tried MAOIs previously, and MAOIs can be useful for TRD [2]. He was instructed about the potential for hypertensive crisis and was given a list of foods to avoid in a tyramine-free diet [3]. His medications (and typical asthma treatments) included phenelzine 75 mg/day, pramipexole 2 mg/day, zolpidem SA 12.5 mg qhs, zolpidem 10 mg qhs, prn prednisone (80 mg decreasing by 10 mg every 3 days) and quetiapine 400 mg/day during tapers. Approximately 4 weeks before admission, he and his wife, a nurse, consulted the internet and read about fibromyalgia and serotonin. Considering that the patient might have fibromyalgia, they added 300 mg of 5-HTP to his medications. They reasoned that, unlike tryptophan, produced through fermentation and potentially contraindicated in a tyramine-free diet, 5-HTP was extracted directly from the seeds of *Griffonia simplicifolia* without fermentation. The web information noted the efficacy of 5-HTP combined with MAOIs

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(pargyline or phenelzine) and the absence of reports of serotonin syndrome induced by 5-HTP.

The patient and spouse noted marked improvement in symptoms of depression immediately upon starting 5-HTP. Less than 2 weeks later, the spouse called to report that she believed that the patient was manic. He could not sleep, and his behavior was erratic. He was told to discontinue the 5-HTP and to take the prescribed quetiapine. The spouse noted improvement upon discontinuation of the 5-HTP. However, during an appointment 5 days later, the patient showed grandiosity, pressured speech, derailment, inattentiveness, insomnia and involvement in many unusual financial concerns. Seven days later, the patient was brought in by the wife because he had developed clear mania and was not manageable at home. He had just terminated a steroid taper begun 1 month earlier for asthmatic exacerbation. Vital signs included temperature=97.5 °F, blood pressure=112/74, pulse rate=94 and respiratory rate=16. He did not have clonus, but his patellar reflexes were hyperactive. There was no flushing, diaphoresis or suggestion of delirium. He was admitted to the hospital with a diagnosis of probable drug-induced mania, ruling out serotonin syndrome. His laboratory evaluation was unremarkable. Vital signs remained stable, but he remained manic despite tapering phenelzine and increasing quetiapine. The patient was uncooperative but not violent. After improving somewhat, he left the hospital against medical advice, not having evidenced imminent risk to himself or to others.

3. Discussion

Many patients believe in alternative medicine and OTC treatments. The widespread availability and use of the internet enable patients' ready access to information of uncertain timeliness and credibility as well as exploitation by the OTC industry. Patients get tempted to become their own doctors.

L-Tryptophan, an essential amino acid, has been used as an OTC supplement to treat a myriad of conditions: insomnia, depression, anxiety, fibromyalgia, etc. However, in 1989, an epidemic of eosinophilia–myalgia syndrome from contaminants in tryptophan supplements involved 1531 cases and 27 deaths [4]. For a period afterward, the sale of tryptophan was prohibited. Tryptophan supplementation became risky and was replaced by 5-HTP as the preferred supplement.

5-Hydroxytryptophan, metabolized from tryptophan via hydroxylation, freely crosses the blood–brain barrier and gets converted to serotonin by aromatic L-amino-acid decarboxylase. This patient took 5-HTP for several reasons: (a) He remained symptomatic with depression. (b) 5-Hydroxytryptophan was not on his list of foods to avoid in a tyramine-free diet. (c) 5-Hydroxytryptophan, unlike tryptophan, was not produced by fermentation, a process that he knew might contain tyramine contraindicated for someone taking an MAOI. (d) The lay literature suggested that 5-HTP was not associated with the serotonin syndrome.

The differential diagnosis included serotonin syndrome and drug-induced mania (MAOI vs. steroid vs. 5-HTP). The combination of tryptophan or 5-HTP with MAOIs can cause a serotonin syndrome/neurotoxicity [5,6]. Furthermore, the combination of 5-HTP with MAOIs or SSRIs in rat models can produce a malignant serotonin syndrome [7,8]. Although this patient had hyperreflexia, he had no other signs or symptoms of serotonin syndrome. Therefore, his provisional diagnosis was drug-induced mania.

Potential culprits for mania were his phenelzine, steroid taper or 5-HTP. The patient remained depressed on phenelzine. He had just completed a prednisone taper and had numerous prior tapers with quetiapine coverage without mania. The timing of the euphoric mood immediately after starting 5-HTP suggests that it was at least a partial precipitant of mania. The "Newcastle cocktail" that combines MAOI, serotonin and lithium is known to have antidepressant effects in severe TRD [9]. Two cases have been reported of inducing hypomania with tryptophan in combination with MAOI [10]. Unlike the present case, we found no reported cases of mania in the setting of 5-HTP added to an MAOI. Clinicians need be alert to such a possibility and emphasize the dangers of OTC supplements especially adjuvant to MAOIs.

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