Tryptophan Precautions

For many decades, tens of millions of people have safely used tryptophan supplements. The mechanisms by which tryptophan functions in the body, however, indicate that those taking certain prescription drugs should exercise caution when using tryptophan on a regular basis.

Although tryptophan has been shown to be safe when used alone, it can potentiate side effects of certain antidepressant drugs. Case reports of serotonin syndrome have noted a connection between tryptophan used concomitantly with monoamine oxidase (MAO) inhibitor drugs. A few popularly prescribed MAO-inhibiting drugs include Nardil® (phenelzine), Parnate® (tranylcypromine), and Marplan® (isocarboxazide). In studies measuring the antidepressant effects of an MAO-inhibitor drug alone compared with that of the MAO inhibitor plus tryptophan, the most common side effects of the combination were dizziness, nausea, and headache. The magnitude of these side effects was sufficient to limit the usefulness of the combination. However, the most serious complication in the use of the combination of tryptophan and MAO inhibitors is the serotonin syndrome. This syndrome is characterized by agitation, restlessness, shivering and tremor, confusion, delirium, tachycardia, diaphoresis, hypomania, myoclonus, hyperreflexia, and blood pressure fluctuations. Although no reports have been published, it is possible that tryptophan, when taken in combination with a selective serotonin-reuptake inhibitor (SSRI) drug such as Prozac®, Paxil®, Zoloft®, or Lexapro®, may also precipitate serotonin syndrome.

The serotonin syndrome was first described in rats. When these animals were given tryptophan plus a monoamine oxidase inhibitor, or various other drugs including high doses of 5-hydroxytryptophan (5-HTP) (with a peripheral decarboxylase inhibitor drug), or serotonin-receptor agonists, the animals exhibited tremor, rigidity, hypertonicity, hind-limb abduction, rigidly arched tail, lateral head shaking, treading movements of the forelimbs, hyperreactivity, myoclonus, and even generalized seizures.

The appearance of the serotonin syndrome in 38 patients in 12 reports has been reviewed. The majority of these cases were associated with patients taking a combination of tryptophan and an MAO-inhibitor drug, but the combination of serotonin-reuptake inhibitor and MAO-inhibitor drugs can also cause the serotonin syndrome. The incidence of the serotonin syndrome in patients is unknown, but some experts argue that it is under-reported, perhaps because it is not recognized, or possibly because it is confused with the neuroleptic malignant syndrome, which has some similarities in terms of symptoms.

The serotonin syndrome usually resolves within 24 hours of cessation of tryptophan treatment, with no residual symptoms. Although the animal model suggests that serotonin antagonists should be a useful treatment, this has not been tested in humans. Supportive measures have been used including cooling for hypothermia, intramuscular chlorpromazine as an antipyretic and sedative, artificial ventilation for respiratory insufficiency, anticonvulsants for seizures, clonazepam for myoclonus, and nifedipine for hypertension.

Although the serotonin syndrome has been reported in patients taking tryptophan and an MAO-inhibitor drug, the incidence of this disorder is low. The total number of patients in the literature reporting symptoms of the serotonin syndrome after taking tryptophan and an MAO-inhibitor drug is less than 40. This is in spite of the fact that tryptophan has been on the market as an antidepressant in the United Kingdom for over 20 years, and psychiatrists in that country are more likely than psychiatrists in North America to use MAO-inhibitor drugs.

Moreover, in the clinical trials on the combination of tryptophan and an MAO-inhibitor drug, there is only one report of symptoms resembling the serotonin syndrome in spite of the very large doses of tryptophan used (up to 18,000 mg of tryptophan per day). There have been no reports of permanent effects after the serotonin syndrome was resolved in patients receiving tryptophan and an MAO-inhibitor drug, although deaths have been seen after the serotonin syndrome in patients who were given MAO-inhibitor and tricyclic antidepressant drugs.
Interaction with Herbs

Tryptophan may cause excessive sedation if it is taken with potentially sedating herbs such as catnip, kava kava, St. John’s wort, or valerian.¹⁹

Warnings and Contraindications

Patients with liver cirrhosis should avoid tryptophan supplementation. Cirrhotic liver disease patients present with reduced activity of tryptophan 2,3-dioxygenase (22%), with subsequent increased free tryptophan and half-life, and decreased clearance." Tryptophan is known to pass into the breast milk of new mothers, but its possible effects in infants are not known. Therefore, tryptophan should also be avoided during breast-feeding. Tryptophan may cause sedation, which may result in sleepiness or mental confusion during the daytime. Individuals who choose to take it should be careful when driving or performing other tasks that require alertness.

Toxicological studies

L-tryptophan has low oral toxicity. A rat carcinogenicity bioassay conducted by the US National Cancer Institute found no evidence of cancer causation.²⁰

Side Effects

Potential side effects of L-tryptophan at high doses (100 mg/kg/day or 7,000 mg taken by a 150-pound person) include gastric irritation, vomiting, and head twitching.²¹ Less severe side effects include:

- Blurry vision • Daytime drowsiness
- Dry mouth • Headaches
- Muscle incoordination • Nausea

Eosinophilia Myalgia Syndrome

In the early 1990s, taking tryptophan was considered to be associated with a severe condition known as eosinophilia myalgia syndrome (EMS).²² Although the exact causes for the outbreak are still not completely known, it is believed that a defective manufacturing process used by one company either introduced contaminants or caused reactions that formed toxic substances within the tryptophan that was produced. However, an independent scientific committee on toxicity recently concluded that tryptophan has not resulted in a detectable increase in risk of EMS, and that pure tryptophan preparations are safe.

References
