



PIC QUESTION OF THE WEEK: 1/3/2005

Q: A possible mechanism for some potential drug interactions is often referred to as the “serotonin syndrome.” What are the key characteristics of the syndrome and what drugs are most often implicated?

A: Serotonin (5-hydroxytryptamine; 5-HT) is a neurotransmitter that plays an important role in sleep-wakefulness, mood, emotional and food behaviors, and thermal regulation. Excessive serotonin activity can result in a constellation of signs and symptoms known as “serotonin syndrome.” It has been classically attributed to combinations of monoamine oxidase inhibitors (MAOIs) and lithium. However, this syndrome can be caused by any combination of drugs that decreases 5-HT metabolism (MAOIs) or re-uptake (SSRIs, other antidepressants, dextromethorphan, meperidine, etc.), or drugs that increase 5-HT release (amphetamines) or act as direct serotonin agonists (Imitrex, etc.). It is the major reason for recommending a 14-day “washout” when discontinuing MAOIs before treatment with SSRIs. Serotonin syndrome is characterized by a triad of signs and symptoms that include mental, autonomic, and neurologic disorders. “Major” symptoms include: confusion, coma, fever, hyperhidrosis, myoclonus, tremors, chills, rigidity, and hyperreflexia. “Minor” symptoms consist of agitation, nervousness, insomnia, tachycardia, tachypnea, dyspnea, diarrhea, low or high blood pressure, impaired coordination, mydriasis, and akathisia. The diagnosis is based on the presence of four “major” symptoms OR three “major” plus two “minor” symptoms. Treatment involves discontinuation of the suspected drug(s), supportive management, and possible treatment with cyproheptadine (a serotonin antagonist), dantrolene, and benzodiazepines.

References:

- Birnes P, Coppin D, Schmitt L, et al. Serotonin syndrome: a brief review. CMAJ 2003;168:1439-42.

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