

**CAN CHLORPHENIRAMINE CAUSE SEROTONIN SYNDROME?**

Dear Sir,

The serotonin syndrome, a rare but serious side effect of drugs that elevate synaptic levels of serotonin, is characterised by a triad of autonomic instability, muscular rigidity and altered sensorium<sup>(1)</sup>. The most serious cases are usually caused by unintended synergism between a selective serotonin reuptake inhibitor (SSRI) and one or more other medications, such as monamine oxidase inhibitors<sup>(1)</sup>. Sometimes, these other offending drugs are not commonly recognised as having serotonergic activity, making diagnosis more difficult. For example, oxycodone<sup>(2)</sup>, bupropion<sup>(3)</sup> and dextromorphan<sup>(4)</sup> have all produced serotonin syndrome when used in combination with SSRIs. Can the common over-the-counter antihistamine chlorpheniramine also produce serotonin syndrome?

Chlorpheniramine was shown in studies from the 1960s to act as a strong serotonin reuptake inhibitor, more potent than tricyclic antidepressants<sup>(5)</sup>. However, this fact has not been widely known and there have been few follow-up studies, making it possible that serotonin syndrome associated with chlorpheniramine could go unrecognised. Labelling for chlorpheniramine typically warns about interactions with monamine oxidase inhibitors and “tranquilisers”, but not SSRIs or serotonin syndrome. Retrospective case studies should be undertaken to look for chlorpheniramine-induced serotonin syndrome. In the meantime, physicians, pharmacists and clinical pharmacologists should keep the possibility of serotonin syndrome in mind when faced with patients taking chlorpheniramine and who present with characteristic findings, and anyone with such cases should publish them in Medline-referenced journals, ideally with internet free full-text access, so that the information will be widely disseminated throughout the world.

Yours sincerely,

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