

CAN CHLORPHENIRAMINE CAUSE SEROTONIN SYNDROME?

Dear Sir,

I read with great interest the recently-published Letter to the Editor by Alisky JM in the Singapore Medical Journal, regarding the possibility of a serotonin syndrome brought about by the use of chlorpheniramine,⁽¹⁾ and I really find the issue very interesting. However, I would like to comment briefly on this report.

Indeed, the so-called “serotonin syndrome” (SS) is a condition of central and peripheral serotonergic hyperstimulation, which is caused by the administration of one or more drugs possessing serotonergic activity. Moreover, in support of a role in receptor specificity, it has been shown that the symptoms observed in the SS are mediated mainly via stimulation of postsynaptic 5-HT_{1A} and possibly 5-HT₂ serotonergic receptors in the central nervous system (CNS).^(2,3) In that context, substances possessing 5-HT_{1A} and/or 5-HT₂ agonistic properties in the CNS could be incriminated for the production of SS. Accordingly, 8-hydroxy-2-(*d-n*-propylamino) tetralin (8-OH-DPAT), a selective 5-HT_{1A} receptor agonist, is well established to produce a SS in rats.⁽⁴⁾

As Dr Alisky refers, the antihistamine chlorpheniramine (CPA) was shown to be a strong serotonin reuptake inhibitor, already in studies conducted in the 1960s. However, and most importantly, in a recent work of our laboratory team, it was demonstrated for the first time that CPA is also a postsynaptic 5-HT_{1A} receptor agonist, producing several aspects of the SS in rats, such as hyperlocomotion and hypothermia.⁽⁵⁾ In this point of view, being a postsynaptic 5-HT_{1A} receptor agonist, CPA fulfils one of the conditions that are essential for substances to be considered as potentially producing a SS. As such, we believe that Dr Alisky should refer this study in his letter, in order to strengthen his assumption towards an implication of CPA in the production of a SS, in cases of concomitant use of this antihistamine with other serotonin-active medications.

Yours sincerely,

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REFERENCES

1. Alisky JM. Can chlorpheniramine cause serotonin syndrome? Singapore Med J 2006; 47:1014.
2. Sternbach H. The serotonin syndrome. Am J Psychiatry 1991; 148:705-13. Comment in: Am J Psychiatry 1992; 149:1116-7, Am J Psychiatry 1992; 149:411-2, Am J Psychiatry 1993; 150:522. Gillman PK. The serotonin syndrome and its treatment. J Psychopharmacol 1999; 13:100-9. Comment in: J Psychopharmacol 2002; 16:191.
3. Gillman PK. The serotonin syndrome and its treatment. J Psychopharmacol 1999; 13:100-9. Comment in: J Psychopharmacol 2002; 16:191.
4. Blanchard RJ, Shepherd JK, Armstrong J, Tsuda SF, Blanchard DC. An ethopharmacological analysis of the behavioral effects of 8-OH-DPAT. Psychopharmacology (Berl) 1993; 112:55-63.
5. Karamanakos PN, Pappas P, Marselos M. Involvement of the brain serotonergic system in the locomotor stimulant effects of chlorpheniramine in Wistar rats: implication of postsynaptic 5-HT_{1A} receptors. Behav Brain Res 2004; 148:199-208.