

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,

Petros N Karamanakos

Department of Neurosurgery
University Hospital of Kuopio
Puijonlaaksontie 2
Kuopio SF-70211
Finland

Tel: (358) 44 024 6835

Fax: (358) 17 173 916

Email: me00188@cc.uoi.gr; petros.karamanakos@kuh.fi

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