Most Antihistamines Cause Some Cognitive Impairment

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — Fexofenadine is the sole truly nonsedating antihistamine—and the only one that does not cause objectively measurable cognitive and psychomotor impairment at doses that are commonly used in clinical practice, said Dr. Kazuhiro Yanai.

Fexofenadine (Allegra) is the only antihistamine that does not permeate the blood-brain barrier and therefore cannot bind to CNS histamine, (H1) receptors, explained Dr. Yanai, professor of pharmacology at Tohoku University, Sendai (Japan), at an international investigative dermatology meeting.

He is credited as a pioneer in utilizing PET scanning to measure brain H1 occupancy by antihistamines and in demonstrating that this measurement correlates with the degree of cognitive and psychomotor impairment.

Dr. Yanai categorizes antihistamines into three categories, which includes antihistamines that cross the blood-brain barrier even at supertherapeutic doses, the "less sedating" antihistamines, which occupy roughly 20% or less of available cortical H1 receptors and are associated with little cognitive impairment at their approved doses; and "more sedating" antihistamines, which bind to 50% or more of brain H1 receptors at recommended doses.

The first-generation antihistamines belong in the more sedating category. The piperazine, which Dr. Yanai called "the most sedating antihistamine ever made," he has shown that a 1-mg oral dose of ketotifen results in a 72% brain H1 occupancy rate (Br. J. Clin. Pharmacol. 2006:61:16-26).

Second-generation antihistamines, with the exception of fexofenadine, fall into the less atating category, he continued.

Another speaker at the Sanofi-Aventis-sponsored symposium, Dr. Ian Hindmarch, professor emeritus of psychopharmacology at the University of Surrey (England), said, "I like to make the analogy to pregnancy. Women are either pregnant or not pregnant. There is no such thing as being a little bit pregnant. Just the same, there’s no such thing as being a little bit impaired. Even a slight degree of impairment can cause an accident if the circumstances are present. All impairment is impairment, and it is only the circumstances—the child who runs into the street—that determines whether that impairment is going to damage you," he asserted.

It is well established that a person can experience quantifiable antihistamine-induced impairment of memory, attention, reaction time, decisiveness, and psychomotor coordination without feeling sleepy or drowsy, according to Dr. Hindmarch. And while such impairment may be less evident with many of the second-generation antihistamines when prescribed at the doses approved for seasonal allergic rhinitis, these agents are often used at far higher, even heroic, doses in treating a variety of pruritic dermatologic diseases.

For example, the standard dosing of cetirizine (Zyrtec) or loratidine (Claritin) for allergic rhinitis is 10 mg/d, but a dosage of 40-50 mg/d is often required to achieve clinical efficacy in patients with idiopathic urticaria or atopic dermatitis. And brain H1 receptor occupancy as well as impairment of superior cognitive functions are antihistamine dose dependent. Dr. Hindmarch stressed at the meeting the importance of knowing one’s patients' drug susceptibility patterns differ considerably, and you may need this information to determine the best therapy for your patient."