Antihistamines are common OTC medications used alone or in combination with other medications. They have a variety of uses such as motion sickness, allergy related symptoms, cough and cold preparations, and as sleep aids. Occasionally, these medications are abused for their hallucinogenic effects.

There are two major classes of antihistamine receptor blockers, H1 and H2. First generation or sedating antihistamines are H1 receptor blockers. They are structurally related to histamine and antagonize the effect of histamine on H1 receptor sites causing therapeutic effects. The “non-sedating” agents or 2nd generation antihistamines are associated with less toxicity as they do not cross the blood-brain barrier as readily as the first generation antihistamines. These agents include: cetirizine, levocetirizine, loratadine, desloratadine, and fexofenadine. The H2 receptor blockers (cimetidine, ranitidine, and famotidine) inhibit gastric acid secretion but otherwise share no effects with the H1 agents.

First generation antihistamines also have anticholinergic effects. For background information, cholinergic effects are responsible for secretions and sweating, increased GI motility, sphincter release (e.g. opening of the lower esophageal sphincter), pupil constriction and slowing of heart rate. Cholinergic receptors in the brain help regulate the level of consciousness and perception. Overdoses of first generation antihistamines cause the opposite effects which are flushed skin, dry mouth, urinary retention, mydriasis, blurred vision, delirium, hallucinations, confusion, agitation, hyperthermia, and tachycardia. (Red as a beet, Dry as a bone, Blind as a bat, Mad as a wet hen, Hot as a hare and Now that's “tacky”). Children are more sensitive to these toxic effects of antihistamines than adults. Some first generation agents (e.g. diphenhydramine) also have local anesthetic and sodium channel blocking effects in large doses.

Diagnosis is generally based on history and can be confirmed by the presentation of the anticholinergic toxidrome.

Anticholinergic Toxidrome: Somnolence, anticholinergic effects stated above, tachycardia, hypertension, agitation, confusion, hallucinations, psychosis, seizures, coma, QRS prolongation and myocardial depression similar to a tricyclic antidepressant overdose (sodium channel blockade), QTc prolongation, and even torsades de pointes (generally occurring in adults with large overdoses).

For specific treatment recommendations for antihistamine overdoses, call the IPCC at 1-800-222-1222

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