07 - 29.7 Antihistamines

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Freeman R, Durso-Decruz E, Emir B. Efficacy, safety, and tolerability of pregabalin treatment for painful diabetic peripheral neuropathy: Findings from seven randomized, controlled trials across a range of doses. Diabetes Care. 2008;31:1448. Frye MA, Ketter TA, Kimbrell TA, Dunn RT, Speer AM. A placebo-controlled study of lamotrigine and gabapentin monotherapy in refractory mood disorders. J Clin Psychopharmacol. 2000;20(6):607. Gadde KM, Franciscy DM, Wagner HR 2nd, Krishnan KR. Zonisamide for weight loss in obese adults: A randomized controlled trial. JAMA. 2003;289(14):1820. Grunze H, Erfurth A, Marcuse A, Amann B, Normann C. Tiagabine appears not to be efficacious in the treatment of acute mania. J Clin Psychiatry. 1999;60(11):759. Hoopes SP, Reimherr FW, Hedges DW, Rosenthal NR, Kamin M. Treatment of bulimia nervosa with topiramate in a randomized, double-blind, placebo-controlled trial, part 1: Improvement in binge and purge measures. J Clin Psychiatry. 2003;64(11):1335. Johnson BA, Rosenthal N, Capece JA. Improvement of physical health and quality of life of alcohol-dependent individuals with topiramate treatment: US multisite randomized controlled trial. Arch Intern Med. 2008;168:1188. Johnson BA, Rosenthal N, Capece JA, Wiegand F, Mao L. Topiramate for treating alcohol dependence: A randomized controlled trial. JAMA. 2007;298(14):1641. Ketter TA, Wang PW. Anticonvulsants: Gabapentin, levetiracetam, pregabalin, tiagabine, topiramate, zonisamide. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock’s Comprehensive Textbook of Psychiatry. 9th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:3021. Klitgaard H. Epilepsy therapy: Anticonvulsants, lessons learned and unmet medical needs. Expert Rev Neurother. 2013;13(1):13–14. Kushner SF, Khan A, Lane R, Olson WH. Topiramate monotherapy in the management of acute mania: Results of four double-blind placebo-controlled trials. Bipolar Disord. 2006;8(1):15. McElroy SL, Hudson JI, Capece JA, Beyers K, Fisher AC. Topiramate for the treatment of binge eating disorder associated with obesity: A placebo-controlled study. Biol Psychiatry. 2007;61(9):1039. McElroy SL, Kotwal R, Guerdjikova AI, Welge JA, Nelson EB. Zonisamide in the treatment of binge eating disorder with obesity: A randomized controlled trial. J Clin Psychiatry. 2006;67(12):1897. Mease PJ, Russell IJ, Arnold LM. A randomized, double-blind, placebo-controlled, phase III trial of pregabalin in the treatment of patients with fibromyalgia. J Rheumatol. 2008;35:502. Perucca P, Mula M. Antiepileptic drug effects on mood and behavior: Molecular targets. Epilepsy Behav. 2013;26(3):440– 449. 29.7 Antihistamines Antihistamines are frequently used in the treatment of a variety of psychiatric disorders because of their sedative and anticholinergic activities. Certain antihistamines (antagonists of histamine H1 receptors) are used to treat neuroleptic-induced parkinsonism and neuroleptic-induced acute dystonia and as hypnotics and anxiolytics. Diphenhydramine (Benadryl) is used to treat neuroleptic-induced parkinsonism and neuroleptic-induced acute dystonia and sometimes as a hypnotic. Hydroxyzine hydrochloride (Atarax) and hydroxyzine pamoate (Vistaril)

are used as anxiolytics. Promethazine (Phenergan) is used for its sedative and anxiolytic effects.

Cyproheptadine (Periactin) has been used for the treatment of anorexia nervosa and inhibited male and female orgasms caused by serotonergic agents. The antihistamines most commonly used in psychiatry are listed in Table 29.7-1. Second-generation, “nonsedating” H1 blockers, such as fexofenadine (Allegra), loratadine (Claritin), and cetirizine (Zyrtec) are less commonly used in psychiatric practice. The newer H2receptor antagonists, such as cimetidine, work primarily on gastric mucosa, inhibiting gastric secretion. Table 29.7-1 Histamine Antagonists Commonly Used in Psychiatry Table 29.7-2 lists antihistaminic drugs not used in psychiatry but that may have psychiatric adverse effects or drug–drug interactions. Table 29.7-2 Other Histamine Antagonists Often Prescribed PHARMACOLOGICAL ACTIONS The H1 antagonists used in psychiatry are well absorbed from the gastrointestinal (GI) tract. The antiparkinsonian effects of intramuscular (IM) diphenhydramine have their onset in 15 to 30 minutes, and the sedative effects of diphenhydramine peak in 1 to 3 hours. The sedative effects of hydroxyzine and promethazine begin after 20 to 60 minutes and last for 4 to 6 hours. Because all three drugs are metabolized in the liver, persons with hepatic disease, such as cirrhosis, may attain high plasma concentrations with long-term administration. Cyproheptadine is well absorbed after oral administration, and its metabolites are excreted in the urine. Activation of H1 receptors stimulates wakefulness; therefore, receptor antagonism causes sedation. All four agents also possess some antimuscarinic cholinergic activity. Cyproheptadine is unique among the drugs because it has both potent antihistamine and serotonin 5-HT2-receptor antagonist properties.

THERAPEUTIC INDICATIONS Antihistamines are useful as a treatment for neuroleptic-induced parkinsonism, neuroleptic-induced acute dystonia, and neuroleptic-induced akathisia. They are an alternative to anticholinergics and amantadine for these purposes. The antihistamines are relatively safe hypnotics, but they are not superior to the benzodiazepines, which have been much better studied in terms of efficacy and safety. The antihistamines have not been proven effective for long-term anxiolytic therapy; therefore, the benzodiazepines, buspirone (BuSpar), or selective serotonin reuptake inhibitors (SSRIs) are preferable for such treatment. Cyproheptadine is sometimes used to treat impaired orgasms, especially delayed orgasm resulting from treatment with serotonergic drugs. Because it promotes weight gain, cyproheptadine may be of some use in the treatment of eating disorders, such as anorexia nervosa. Cyproheptadine can reduce recurrent nightmares with posttraumatic themes. The antiserotonergic activity of cyproheptadine may counteract the serotonin syndrome caused by concomitant use of multiple serotonin-activating drugs, such as SSRIs and monoamine oxidase inhibitors. PRECAUTIONS AND ADVERSE REACTIONS Antihistamines are commonly associated with sedation, dizziness, and hypotension, all of which can be severe in elderly persons, who are also likely to experience the anticholinergic effects of those drugs. Paradoxical excitement and agitation is an adverse effect seen in a small number of persons. Poor motor coordination can result in accidents; therefore, persons should be warned about driving and operating dangerous machinery. Other common adverse effects include epigastric distress, nausea, vomiting, diarrhea, and constipation. Because of mild anticholinergic activity, some people experience dry mouth, urinary retention, blurred vision, and constipation. For this reason also, antihistamines should be used only at very low doses, if at all, by persons with narrow-angle glaucoma or obstructive GI, prostate, or bladder conditions. A central anticholinergic syndrome with psychosis may be induced by either cyproheptadine or diphenhydramine. The use of cyproheptadine in some persons has been associated with weight gain, which may contribute to

its reported efficacy in some persons with anorexia nervosa. In addition to the above adverse effects, antihistamines have some potential for abuse. The coadministration of antihistamines and opioids can increase the euphoria experienced by persons with substance dependence. Overdoses of antihistamines can be fatal. Antihistamines are excreted in breast milk, so their use should be avoided by nursing mothers. Because of some potential for teratogenicity, pregnant women should avoid the use of antihistamines. DRUG INTERACTIONS The sedative property of antihistamines can be additive with other central nervous system (CNS) depressants, such as alcohol, other sedative–hypnotic drugs, and many

psychotropic drugs, including tricyclic drugs and dopamine receptor antagonists (DRAs). Anticholinergic activity can also be additive with that of other anticholinergic drugs and may sometimes result in severe anticholinergic symptoms or intoxication. LABORATORY INTERFERENCES H1 antagonists may eliminate the wheal and induration that form the basis of allergy skin tests. Promethazine may interfere with pregnancy tests and may increase blood glucose concentrations. Diphenhydramine may yield a false-positive urine test result for phencyclidine (PCP). Hydroxyzine use can falsely elevate the results of certain tests for urinary 17-hydroxycorticosteroids. DOSAGE AND CLINICAL GUIDELINES The antihistamines are available in a variety of preparations (Table 29.7-3). IM injections should be deep, because superficial administration can cause local irritation. Table 29.7-3 Dosage and Administration of Common Histamine Antagonists Intravenous (IV) administration of 25 to 50 mg of diphenhydramine is an effective treatment for neuroleptic-induced acute dystonia, which may immediately disappear. Treatment with 25 mg three times a day—up to 50 mg four times a day, if necessary— can be used to treat neuroleptic-induced parkinsonism, akinesia, and buccal movements. Diphenhydramine can be used as a hypnotic at a 50 mg dose for mild transient insomnia. Doses of 100 mg have not been shown to be superior to doses of 50 mg, but they produce more anticholinergic effects than doses of 50 mg.

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