04 - 29.4 b Adrenergic Receptor Antagonists

29.4 b-Adrenergic Receptor Antagonists

Hollander E, Petras JN. α2-Adrenergic receptor agonists: Clonidine and guanfacine. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:3004. Karachalios GN, Charalabopoulos A, Papalimneou V, Kiortsis D, Dimicco P. Withdrawal syndrome following cessation of antihypertensive drug therapy. Int J Clin Pract. 2005;5:562. Kornfield R, Watson S, Higashi AS, Conti RM, Dusetzina SB, Garfield CF, Dorsey ER, Huskamp HA, Alexander GC. Effects of FDA advisories on the pharmacologic treatment of ADHD, 2004–2008. Psychiatr Serv. 2013;64(4):339–346. Marsch LA, Bickel WK, Badger GJ, Stothart ME, Quesnel KJ. Comparison on pharmacological treatments for opioiddependent adolescents: A randomized controlled trial. Arch Gen Psychiatry. 2005;62:1157. Ming X, Gordon E, Kang N, Wagner GC. Use of clonidine in children with autism spectrum disorders. Brain Dev. 2008;30(7):454. Myers SM. The status of pharmacotherapy for autism spectrum disorders. Expert Opin Pharmacother. 2007;8(11):1579. Sallee F, Connor DF, Newcorn JH. A review of the rationale and clinical utilization of 2-adrenoceptor agonists for the treatment of attention-deficit/hyperactivity and related disorders. J Child Adolesc Psychopharmacol. 2013;23(5):308– 319. 29.4 β-Adrenergic Receptor Antagonists Because of the innervations of many, if not most, peripheral organs and vasculature by the sympathetic division of the autonomic nervous system, their functions are ultimately controlled, in part, by one of the two major classes of adrenergic receptors: α-receptors (discussed in Section 29.3) and β-receptors. These receptors are further subdivided based on their action and location, and they are located both peripherally and in the central nervous system (CNS). Shortly after being introduced for cardiac indications, propranolol (Inderal) was reported to be useful for agitation, and its use in psychiatry spread rapidly. The five most commonly used β-receptor antagonists in psychiatry are propranolol, nadolol (Corgard), metoprolol (Lopressor, Toprol), pindolol (Visken), and atenolol (Tenormin) (Table 29.4-1). Table 29.4-1 β-Adrenergic Drugs Used in Psychiatry

PHARMACOLOGIC ACTIONS The β-receptor antagonists differ with regard to lipophilicities, metabolic routes, βreceptor selectivity, and half-lives. The absorption of the β-receptor antagonists from the gastrointestinal tract is variable. The agents that are most soluble in lipids (i.e., are

lipophilic) are likely to cross the blood–brain barrier and enter the brain; those agents that are least lipophilic are less likely to enter the brain. When CNS effects are desired, a lipophilic drug may be preferred; when only peripheral effects are desired, a less lipophilic drug may be indicated. Whereas propranolol, nadolol, pindolol, and labetalol (Normodyne, Trandate) have essentially equal potency at both the β1- and β2-receptors, metoprolol and atenolol have greater affinity for the β1-receptor than for the β2-receptor. Relative β1-selectivity confers few pulmonary and vascular effects of these drugs, although they must be used with caution in persons with asthma because the drugs retain some activity at the β2receptors. Pindolol has sympathomimetic effects in addition to its β-antagonist effects, which has allowed its use for augmentation of antidepressant drugs. Pindolol, propranolol, and nadolol possess some antagonist activity at the serotonin 5-HT1A receptors. THERAPEUTIC INDICATIONS Anxiety Disorders Propranolol is useful for the treatment of social phobia, primarily of the performance type (e.g., disabling anxiety before a musical performance). Data are also available for its use in treatment of panic disorder, posttraumatic stress disorder, and generalized anxiety disorder. In social phobia, the common treatment approach is to take 10 to 40 mg of propranolol 20 to 30 minutes before the anxiety-provoking situation. The βreceptor antagonists are less effective for the treatment of panic disorder than are benzodiazepines or selective serotonin reuptake inhibitors (SSRIs). Lithium-Induced Postural Tremor The β-receptor antagonists are beneficial for lithium-induced postural tremor and other medication-induced postural tremors—for example, those induced by tricycle antidepressants (TCAs) and valproate (Depakene). The initial approach to this movement disorder includes lowering the dose of lithium (Eskalith), eliminating aggravating factors, such as caffeine, and administering lithium at bedtime. If these interventions are inadequate, however, propranolol in the range of 20 to 160 mg a day given two or three times daily is generally effective for the treatment of lithium-induced postural tremor. Neuroleptic-Induced Acute Akathisia

Many studies have shown that β-receptor antagonists can be effective in the treatment of neuroleptic-induced acute akathisia. They are generally more effective for this indication than are anticholinergics and benzodiazepines. The β-receptor antagonists are not effective in the treatment of such neuroleptic-induced movement disorders as acute dystonia and parkinsonism. Aggression and Violent Behavior The β-receptor antagonists may be effective in reducing the number of aggressive and violent outbursts in persons with impulse disorders, schizophrenia, and aggression associated with brain injuries such as trauma, tumors, anoxic injury, encephalitis, alcohol dependence, and degenerative disorders (e.g., Huntington’s disease). Alcohol Withdrawal Propranolol is reported to be useful as an adjuvant to benzodiazepines but not as a sole agent in the treatment of alcohol withdrawal. The following dose schedule is suggested: no propranolol for a pulse rate below 50 beats per minute; 50 mg propranolol for a pulse rate between 50 and 79 beats per minute; and 100 mg propranolol for a pulse rate of 80 beats per minute or above. Antidepressant Augmentation Pindolol has been used to augment and hasten the antidepressant effects of SSRIs, tricyclic drugs, and electroconvulsive therapy. Small studies have shown that pindolol administered at the onset of antidepressant therapy may shorten the usual 2- to 4-week latency of antidepressant response by several days. Because the β-receptor antagonists may possibly induce depression in some persons, augmentation strategies with these drugs need to be further clarified in controlled trials. Other Disorders A number of case reports and controlled studies have reported data indicating that βreceptor antagonists may be of modest benefit for persons with schizophrenia and manic symptoms. They have also been used in some cases of stuttering (Table 29.4-2). Table 29.4-2 Psychiatric Uses for β-Adrenergic Receptor Antagonists

PRECAUTIONS AND ADVERSE REACTIONS The β-receptor antagonists are contraindicated for use in people with asthma, insulindependent diabetes, congestive heart failure, significant vascular disease, persistent angina, and hyperthyroidism. The contraindication in diabetic persons is because of the drugs' antagonizing the normal physiologic response to hypoglycemia. The β-receptor antagonists can worsen atrioventricular (AV) conduction defects and lead to complete AV heart block and death. If the clinician decides that the risk-to-benefit ratio warrants a trial of a β-receptor antagonist in a person with one of these coexisting medical conditions, a β1-selective agent should be the first choice, and the patient should be monitored. All currently available β-receptor antagonists are excreted in breast milk and should be administered with caution to nursing women. The most common adverse effects of β-receptor antagonists are hypotension and bradycardia. In persons at risk for these adverse effects, a test dosage of 20 mg a day of propranolol can be given to assess the reaction to the drug. Depression has been associated with lipophilic β-receptor antagonists, such as propranolol, but it is probably rare. Nausea, vomiting, diarrhea, and constipation can also be caused by treatment with these agents. The β-receptor antagonists may blunt cognition in some people. Serious CNS adverse effects (e.g., agitation, confusion, and hallucinations) are rare. Table 29.43 lists the possible adverse effects of β-receptor antagonists. Table 29.4-3 Adverse Effects and Toxicity of β-Adrenergic Receptor Antagonists

DRUG INTERACTIONS Concomitant administration of propranolol results in increases in plasma concentrations of antipsychotics, anticonvulsants, theophylline (Theo-Dur, Slo-bid), and levothyroxine (Synthroid). Other β-receptor antagonists may have similar effects. The β-receptor antagonists that are eliminated by the kidneys may have similar effects on drugs that are also eliminated by the renal route. Barbiturates, phenytoin (Dilantin), and cigarette smoking increase the elimination of β-receptor antagonists that are metabolized by the liver. Several reports have associated hypertensive crises and bradycardia with the coadministration of β-receptor antagonists and monoamine oxidase inhibitors. Depressed myocardial contractility and AV nodal conduction can occur from concomitant administration of a β-receptor antagonist and calcium channel inhibitors. LABORATORY INTERFERENCES The β-receptor antagonists do not interfere with standard laboratory tests. DOSAGE AND CLINICAL GUIDELINES Propranolol is available in 10-, 20-, 40-, 60-, 80-, and 90-mg tablets; 4-, 8-, and 80mg/mL solutions; and 60-, 80-, 120-, and 160-mg sustained-release capsules. Nadolol is available in 20-, 40-, 80-, 120-, and 160-mg tablets. Pindolol is available in 5- and 10-mg

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