Common Medications Prescribed for Adolescent Dental Patients

Paul A. Moore, DMD, PhD, MPH[a],[*],
Elliot V. Hersh, DMD, MS, PhD[b]

[a]School of Dental Medicine, University of Pittsburgh, 3501 Terrace Street,
552 Salk Hall, Pittsburgh, PA 15261, USA
[b]School of Dental Medicine, University of Pennsylvania, 240 South 40th Street,
The Robert Schattner Center, Philadelphia, PA 19104-6030, USA

Adolescent patients may present to a dental practitioner's office with an array of behavioral, developmental, dental, and medical challenges. Although medications taken by teenagers are often distinct from adult therapies, there is little to indicate that pharmacokinetic dynamics are significantly different during adolescence. It is fortunate that variations in absorption, distribution, and elimination reported with infants are not reported among teenage patients. Hepatic P-450 drug metabolism is known to be underdeveloped in newborns. During the years between toddler age and the beginning of puberty, drug metabolism capacity is usually elevated and generally greater than that seen in adulthood. During the teenage years, hepatic drug metabolizing functions slowly decline to adult levels [1].

Off-label use of prescription medications to treat children and adolescents is common in medical practice. It is unfortunate that clinical research studies for establishing drug efficacy and safety in children are not routinely required by the Food and Drug Administration (FDA), and when studies are mandated for a specific indication, they are difficult to perform due to ethical and legal concerns. Definitive clinical data of efficacy and safety frequently are incomplete. Without comprehensive clinical trials, it is difficult to ensure that children are not being placed at unnecessary risk. Avoiding the use of prescription drugs, however, may be depriving children of potentially effective medicines [2].

* Corresponding author.
E-mail address: pam7@pitt.edu (P.A. Moore).

Psychopharmacologic agents

The use of psychopharmacologic medications to treat behavioral and psychologic disorders in children is extremely controversial. Nonpharmacologic strategies to manage childhood psychologic disorders such as attention-deficit/hyperactivity disorder (ADHD), depression, general anxiety disorders, and obsessive-compulsive disorders (OCD) are always preferred. Effective, disorder-specific cognitive and behavior therapies have been established for most childhood psychologic disorders and should always be the first choice for therapy.

When necessary, various central nervous system stimulant medications have proved to be effective for managing ADHD. The primary agents are methylphenidate and related amphetamines; various derivatives of these stimulants also are currently available (Box 1). Most notably, long-acting formulations, designed to last throughout the school day, are now available.

Box 1. Commonly prescribed psychopharmacologic agents

Antidepressants—selective serotonin reuptake inhibitors
Citalopram (Celexa)
Escitalopram (Lexapro)
Fluoxetine (Prozac)
Paroxetine (Paxil)
Sertraline (Zoloft)
Venlafaxine (Effexor)

Obsessive compulsive disorders
Paroxetine (Paxil)
Clomipramine (Anafranil)
Amitriptyline

Attention-deficit/hyperactivity disorder medications
Methylphenidate (Ritalin)
Methylphenidate/long acting (Concerta, Metadate)
Dexmethylphenidate (Focalin)
Dextroamphetamine (Dexadrine)
Amphetamine mixtures (Adderall)
Pemoline (Cylert)
Atomoxetine (Strattera)

Migrainous headaches
Propranolol (Inderal)
Amitriptyline
Divalproex (Depakote)
Sumatriptan (Imitrex)

Side effects of ADHD medications include anorexia, headaches, and abdominal pain. Elevated blood pressure and heart rate have been reported for some children using these stimulants. For children with elevated blood pressures, caution is indicated when administering local anesthetics containing vasoconstrictors, although a definitive adverse interaction between ADHD medications and dental vasoconstrictors has not been demonstrated. Administering a local anesthetic formulation containing no epinephrine or levonordefrin vasoconstrictor, such as 3% mepivacaine is a rational alternative for these patients.

The popularity of the selective serotonin reuptake inhibitors (SSRIs) to treat depression can be attributed, in part, to the lack of serious side effects reported previously when taking major psychosedative antidepressants agents such as the tricyclic antidepressant agents and monoamine oxidase inhibitors. The three most popular SSRIs taken orally are sertraline, fluoxetine, and paroxetine [3]. These agents are used to manage depression and severe generalized anxiety disorders in adolescence. In addition, sertraline has FDA approval specifically for the treatment of OCD in children. Few comparative trials of the relative efficacy of these agents have been reported. A meta-analysis of medications for OCD indicates that the tricyclic antidepressant clomipramine may be more effective than SSRIs [4].

Although SSRIs are approved for the treatment of depression in children, long-term safety questions regarding personality and behavioral development have not been completely resolved. Increased thoughts of suicide and attempted suicide in children and adolescents have been reported. Of note, the same warning recently has been reported for the ADHD medication, atomoxitene. Although still under debate, many believe that the use of SSRIs to treat depression is likely to prevent more suicides than they may cause [5]. Because of the ability of SSRIs to inhibit various cytochrome P-450 drug metabolizing enzymes (2C9, 2C19, 2D6), these drugs can theoretically increase blood levels of diazepam and various nonsteroidal anti-inflammatory drugs. In addition, because the narcotic analgesics codeine and tramadol are prodrugs activated by CYP2D6, SSRIs could impair their analgesic action [6].

Recurring headaches are a common complaint among teenagers. Migrainous headaches, most frequently reported by adolescent girls, may require pharmacologic management. Agents used to prevent recurring headaches include the nonselective β-blockers propranolol, tricyclic antidepressants (amitriptyline), and topiramate. Management of acute headache episodes often relies on the selective serotonin agonist sumatriptan [2].

Vasoconstrictors should be used cautiously with patients currently taking nonselective β-adrenoreceptor antagonists and tricyclic antidepressants. Patients taking nonselective β-adrenergic antagonists such as propranolol may experience exaggerated systemic vasoconstrictive responses to epinephrine or levonordefrin. If a reaction does result from local anesthetic administration, then treatment recommendations include monitoring vital signs,

explaining to the patient the cause of the symptoms, and reassuring the patient that the response will last only a few minutes. If a significant rise in blood pressure is noted, then definitive drug treatment in a dental office is sublingual nitroglycerin and immediate transport to the local hospital emergency room [7,8].

The major psychosedatives such as the tricyclic antidepressants and monoamine oxidase inhibitors are prescribed rarely to teenagers because of serious side effects and drug interactions. Reports of xerostomia are common with these agents, and significant hyposalivation may increase the risk for dental caries. In addition, exaggerated depressant responses are possible when patients who are taking major psychosedatives are prescribed opioid analgesics or central nervous system sedatives.

Management of skin disorders

Facial acne is a common and often devastating disorder for an adolescent. Although severity varies, 85% of adolescents experience acne at some time during their teenage years. As indicated in Box 2, systemic treatments may include antibiotic therapy and, in girls, oral contraceptive steroids. The antibiotics most often prescribed, tetracycline or erythromycin, are often administered long-term when treating acne in adolescent patients. The dental concerns and treatment impacts for antibiotics and contraceptives are discussed later. If the acne is severe, then isotretinoin, a derivative of vitamin A that suppresses the activity of sebaceous glands, may be offered by the child's dermatologist.

Isotretinoin is extremely effective in treating cystic facial lesions and may lead to prolonged remissions. The course of treatment with isotretinoin may last from 3 to 6 months. Dry skin, photosensitivity, and chelitis commonly are reported with its use. The most serious reactions to isotretinoin are well-documented teratogenicity. Psychologic side effects including depression and psychoses are also possibly associated with its use [9]. Careful monitoring of the adolescent's behavior and psychologic state and the prevention of pregnancy are mandatory [10].

Box 2. Common prescriptions for skin disorders

Isotretinoin (Accutane)
Tretinoin cream (Retin-A, Avita)
Adapalene cream (Differin)
Benzoyl peroxide (Benzac)
Clindamycin topical (Cleocin-T)
Doxycycline (Vibramycin)
Oral contraceptives (Ortho-Cept)

Pulmonary drugs

Adolescent asthma is an airway inflammation characterized by reversible airway obstruction and an increased responsiveness to a variety of stimuli. Nearly 10% of adolescents will experience symptoms of the disease at some time. As shown in Box 3, preventative treatment involves limiting inflammation by administering corticosteroids, mast cell stabilizers, leukotriene receptor antagonists, and bronchodilators (theophylline, β_2-receptor agonists, and others). Rapid-acting β_2-adrenergic receptor agonists such as albuterol are used to manage acute reactions, whereas long-acting β_2-adrenergic receptor agonists such as salmeterol are used for prevention. Combination therapies are sometimes the most effective treatment [11,12].

Adverse reactions associated with theophylline are generally mild when peak serum theophylline concentrations are less than 20 µg/mL and consist mainly of transient caffeine-like adverse effects such as nausea, vomiting, headache, and insomnia. When peak serum theophylline concentrations exceed 20 µg/mL, however, theophylline produces a wide range of adverse reactions including persistent vomiting, cardiac arrhythmias, and intractable seizures [2]. Erythromycin is a well-known inhibitor of CYP1A2, the hepatic drug-metabolizing enzyme for theophylline. Coadministration of erythromycin with theophyline may result in a 35% increase in theophyline blood levels and induce toxic reactions [6,13,14].

Box 3. Common prescriptions for treating asthma

Selective β_2-adrenergic receptor agonists
Salmeterol (Serevent)
Albuterol (Proventil)

Glucocorticoids
Beclomethasone (Vaceril)
Budesonide (Pulmicort)
Flunisolide (Aerobid)
Fluticasone (Flovent)
Triamcinolone (Azmacort)

Leukotriene synthesis inhibitors
Montelukast (Singulair)

Methylxanthines
Theophylline (Theo-Dur)

Mast cell stabilizers
Cromolyn (Gastrocrom)

Combination therapies
Salmeterol/fluticasone (Advair)

Sulfite antioxidant preservatives (sulfur dioxide, sulfites, bisulfites, and metabisulfites) have been reported to sensitize some asthmatic patients when they are exposed to large amounts. In fact, as many as 5% of the 9 million asthmatic patients in the United States may be sulfite-sensitive. Reactions of urticaria, angioedema, bronchospasm, and anaphylactic shock have been reported. History of asthma, particularly if sulfite sensitivity is noted, may be important in selecting a local anesthetic agent, because sulfites are contained in epinephrine or levonordefrin formulations. Although some concern and caution is justified when using local anesthetics containing vasoconstrictors and sulfites, well-documented reactions in dental practice are extremely rare, probably because the amount of this antioxidant sulfite in a dental formulation is too small to stimulate a significant life-threatening reaction. Local anesthetic solutions that do not include vasoconstrictors, such as 3% mepivacaine plain and 4% prilocaine plain, may be considered safe alternatives in truly sensitive individuals [8,13].

Antidiabetes agents

Type 1 diabetes mellitus (T1DM) is diagnosed most often before 30 years of age and is characterized by abrupt onset of polyuria (excessive secretion of urine) and polydipsia (excessive or abnormal thirst). In adolescents, T1DM is thought to be due to a complete autoimmune-mediated destruction of the pancreatic β cells; insulin replacement is required for survival (Box 4).

Approximately 5% to 10% of all patients who have diabetes are classified type 1 [15]. Over the past 20 years, there has been a dramatic increase in the prevalence of type 2 diabetes mellitus (T2DM) in youth, particularly among minority populations, with the most pronounced increase in the adolescent

---

Box 4. Common prescriptions for managing diabetes

Antidiabetic agents: oral
Acarbose (Precose)
Metformin (Glucophage)
Glipizide (Glucotrol)
Glyburide (Diabeta, Micronase)
Rosiglitazone (Avandia)
Pioglitazone (Actos)
Metformin/glyburide (Glucovance)

Human insulins
Insulin aspart (Novolog)
Insulin lispro (Humalog)
Regular insulin (Humulin, Novolin)

age group. Investigators attribute this rise to patterns of obesity and lack of physical activity [16].

In general, children who have T1DM who maintain proper glycemic control can receive dental care with minimal adjustments in treatment. Many adolescents who have T1DM carefully monitor their blood glucose and self-administrate incremental doses of insulin throughout the day in an effort to "normalize" their glucose levels (eg, HbA1c < 7%). With intensive insulin management, hypoglycemic reactions are likely to occur more often. Practitioners should optimize their scheduling of appointments and be prepared to manage acute hypoglycemic episodes if they develop.

In adolescence, the most common oral complications associated with T1DM are gingivitis and periodontitis. T2DM in adolescence may be associated with an increased incidence of dental caries. Poor oral hygiene, cigarette smoking, and a higher frequency of between-meal snacking are known risk behaviors [17,18]. Prevention of the oral health sequelae of diabetes relies primarily on health promotion strategies. Dental practitioners should individualize prevention strategies to patient needs, possibly incorporating dietary evaluations and counseling, smoking cessation recommendations, assessment of salivary functions, additional topical fluoride applications, and instructions for proper oral hygiene [19].

The prevalence of heart murmurs among adolescent patients who have T1DM is similar to the prevalence in those who do not have diabetes; however, it has been noted that patients who have T1DM are likely to report a cardiac murmur when completing their health history, possibly because they have had more frequent encounters with their physicians and more heart auscultations. Confirmation of the need for antibiotic prophylaxis before dental care may require medical consultation to rule out possible misdiagnosis of cardiac valvular disease [20].

Contraceptive steroids

Teenage girls may report the use of oral contraceptives when completing the medical questionnaire. These agents, most frequently formulated as combinations of estrogen and progestin, act to prevent ovulation and implantation (Box 5). Although formulated as agents to prevent pregnancy, by modifying estrogen levels, their efficacy in the treatment of acne also has been demonstrated [2].

Teenage girls taking birth control pills may display acute gingivitis, similar to puberty gingivitis, that can usually be managed through meticulous oral hygiene. It has been reported that patients taking oral contraceptive steroids are at a greater risk of alveolar osteitis (dry sockets) following the removal of mandibular third molars. The risk of dry sockets may be decreased by scheduling surgery during the 7-day period when the contraceptive agent is not being taken [21].

Box 5. Common prescriptions for birth control

Estrogen: sole agent
Esclim Transdermal

Progestin/estrogen combinations
Ortho-Novum
Yasmin 28
Ortho-Cept 21
Lo/Ovral 21
Tri-Norinyl 21

An increased incidence of thromboembolism and thrombitis when administering intravenous diazepam has also been demonstrated. Although not supported by clinical trials, concomitant use of antibiotics has been implicated in failure of oral contraceptive steroids [22]. As a medicolegal precaution, it is prudent to caution patients of this unlikely event and to recommend the use of additional forms of birth control, including barrier techniques and abstinence, while taking any antibiotic medication [23].

Antibiotics

The most commonly prescribed antibiotic in the United States is amoxicillin, a semisynthetic antibiotic and analog of ampicillin (Box 6) [1]. It has a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Amoxicillin is often used to treat adolescent patients who have upper respiratory infections and otitis media. In adolescents, amoxicillin is often prescribed as part of an oral formulation containing clavulanic acid.

As reported for other penicillins, untoward reactions are related most commonly to hypersensitivity phenomena. These reactions are likely to occur in individuals who have previously demonstrated hypersensitivity to other penicillins and in those who have a history of allergy, asthma, hay

---

Box 6. Common prescriptions for childhood infections

Amoxicillin (Amoxcil)
Amoxicilln/clavanate (Augmentin)
Clarithromycin (Biaxin)
Azithromycin (Zithromax)
Erythromycin (Ery-Tab)
Clindamycin (Cleocin)

---

fever, or urticaria. Concomitant use of bacteriostatic antibiotics such as the macrolides, sulfonamides, and tetracyclines may theoretically interfere with the bactericidal effects of penicillin. Although this drug interaction has been demonstrated in vitro, the clinical significance of this interaction has not been confirmed.

Azithromycin is an azalide, a subclass of macrolide antibiotics such as erythromycin, used to treat gram-positive infections. Azithromycin acts by binding to the 50S ribosomal subunit of susceptible microorganisms, thus interfering with microbial protein synthesis. Azithromycin concentrates in phagocytes and fibroblasts as demonstrated by in vitro incubation techniques. In vivo studies suggest that concentration in phagocytes may contribute to drug effectiveness in infected tissues [1].

The infections most often treated with azithromycin in adolescents include pharyngitis, tonsillitis, and acute otitis media. Most side effects are related to the gastrointestinal tract (eg, nausea, vomiting, diarrhea, or abdominal pain). Serious allergic reactions including angioedema and anaphylaxis and dermatologic reactions including Stevens-Johnson syndrome have been reported [1]. Clarithromycin is a semisynthetic macrolide antibiotic that has activity similar to erythromycin and azithromycin. In adolescent patients, the most frequently reported side effects are diarrhea, vomiting, abdominal pain, and headache.

The use of erythromycin and clarithromycin in patients concurrently taking drugs metabolized by the cytochrome P450 system may be associated with elevations in serum levels of these other drugs [6]. There have been reports of interactions of erythromycin or clarithromycin with carbamazepine, cyclosporine, tacrolimus, hexobarbital, phenytoin, alfentanil, disopyramide, lovastatin, bromocriptine, valproate, terfenadine, cisapride, pimozide, rifabutin, and astemizole [6,13].

Triazolam, an oral benzodiazepine sedative often recommended for oral anxiolysis before dental care, can reliably decrease anxiety when administered before dental treatment [24]. Erythromycin and clarithromycin have also been reported to decrease the clearance of triazolam and thereby significantly increase the pharmacologic effect of triazolam [6,14]. Oral sedation using triazolam or midazolam, another short-acting benzodiazepine, can result in unexpected oversedation because erythromycin and clarithromycin can decrease clearance of these benzodiazpine sedatives, resulting in somnolence and confusion.

Summary

After initiating treatment of an adolescent patient, a dental practitioner may encounter unique medical disorders and medications not commonly seen in adult populations. It is fortunate that variations in drug absorption, distribution, and elimination are not significant among teenage patients. Some agents present unusual adverse reactions such as the teratogenicity

of isotretinoin and the elevated blood pressure sometimes associated with methylphenidate. Other medications may impact success of dental therapy, such as the increased risk of alveolar osteitis following the removal of mandibular third molars among adolescents taking oral contraceptive steroids. Other medications may induce significant drug interactions important to dental practice, such as the exaggerated central nervous system depression seen when triazolam is administered concomitantly with erythromycin. A thorough understanding of the toxicities, adverse drug reactions, and possible drug interactions associated with the medications prescribed for adolescent dental patients are essential for optimizing dental care.

References

[1] Friedman SB, Fischer M, Schonberg SK, et al, editors. Comprehensive adolescent health care. 2nd edition. St. Louis (MO): Mosby Year Book; 1998.

[2] Cuzzolin L, Zaccaron A, Fanos V. Unlicensed and off-label uses of drugs in paediatrics: a review of the literature. Fund Clin Pharm 2003;17(1):125–31.

[3] RxList: The Internet Drug Index. The top 300 prescriptions for 2004 by number of US prescriptions dispensed. Available at: http://www.rxlist.com/top200.htm. Accessed June 29, 2005.

[4] Geller DA, Biederman J, Stewart SE. Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorders. Am J Psychiatry 2003;60:1919–28.

[5] Are SSRIs safe for children? Med Lett Drugs Ther 2003;45:53–4.

[6] Hersh EV, Moore PA. Drug interactions in dentistry: the importance of knowing your CYP's. J Am Dent Assoc 2004;135:298–311.

[7] Moore PA. Adverse drug interactions in dental practice: interactions associated with local anesthetics, sedatives and anxiolytics. J Am Dent Assoc 1999;130:541–54.

[8] Finder RL, Moore PA. Adverse drug reactions to local anesthesia. Dent Clin North Am 2002;46(4):747–58.

[9] Wysowski DK, Pitts M, Bietz J. Methodological limitations of the study "isotretinoin use and risk of depression, psychotic symptoms, suicide, and attempted suicide." J Am Acad Dermatol 2001;45:515.

[10] Jick SS, Kremers HM, Vasilakis-Scaramozza C. Isotretinoin use and risk of depression, psychotic symptoms, suicide, and attempted suicide. Arch Dermatol 2000;136(10):1231–6.

[11] Shrewsbury S, Pyke S, Britton M. Meta-analysis of increased dose of inhaled steroid or addition of salmeterol in symptomatic asthma (MIASMA). BMJ 2000;320(7246):1368–73.

[12] Nelson HS, Busse WW, Kerwin E, et al. Fluticasone propionate/salmeterol combination provides more effective asthma control than low-dose inhaled corticosteroid plus montelukast. J Allergy Clin Immunol 2000;106(6):1088–95 [erratum in J Allergy Clin Immunol 2001;107(4):614].

[13] Bush RK, Taylor SL, Holden K, et al. Prevalence of sensitivity to sulfatin agents in asthmatic patients. Am J Med 1986;81:816–20.

[14] Moore PA. Erythromycin and the newer long-acting macrolide antibiotics. J Am Dent Assoc 1999;130:1341–3.

[15] Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults: the Third National Health and Nutrition Examination Survey, 1988–1994. Diabetes Care 1998;21:518–24.

[16] Rosenbloom AL, Joe JR, Young RS, et al. Emerging epidemic of type 2 diabetes in youth. Diabetes Care 1999;22:345–54.

[17] Moore PA, Weyant RJ, Mongelluzzo MB, et al. Type 1 diabetes mellitus and oral health: assessment of tooth loss and edentulism. J Dent Public Health 1998;58:135–42.

[18] Moore PA, Weyant RJ, Mongelluzzo MB, et al. Type 1 diabetes mellitus and oral health: assessment of periodontal disease. J Periodont 1999;70:409–17.

[19] Moore PA, Orchard T, Guggenheimer J, et al. Diabetes and oral health promotion: a survey of disease prevention behaviors. J Am Dent Assoc 2000;131:1333–41.

[20] Guggenheimer J, Orchard TJ, Moore PA, et al. Lack of reliability of self-reported heart murmur history: findings from a dental study of insulin-dependent diabetic patients. J Am Dent Assoc 1998;129:861–70.

[21] Cohen ME, Simecek JW. Effects of gender-related factors on the incidence of localized alveolar osteitis. Oral Sug Oral Med Oral Path Oral Radiol Endol 1992;79:416–22.

[22] Hersh EV. Adverse drug interactions in dental practice: interactions involving antibiotics, part II of a series. J Am Dent Assoc 1999;130:236–51.

[23] DeRossi SS, Hersh EV. Antibiotics and oral contraceptives. Dent Clin North Am 2002;46: 653–64.

[24] Stopperich DS, Moore PA, Finder RL, et al. Oral triazolam pretreatment for intravenous sedation. Anesth Prog 1993;40:117–21.