A POTPOURRI OF CLINICAL AND USEFUL DENTAL PHARMACOLOGY

Hosted by the

Greater Kansas City Dental Society

Blue Springs, Missouri February 14, 2020

Are all generic drugs equal?

Orange Book

(Approved Drug Products with Therapeutic Equivalence Evaluations)

Alliance for Safe Online Pharmacies (ASOP)

No. 1 LEVOTHYROXINE (generic)

- Synthroid®
- replacement therapy (hypothyroidism)
 - incidence is about 5% in the U. S.
 - women 9x more likely than men
 - subclinical hypothyroidism
- local anesthetic with vasoconstrictor is **NOT** contraindicated
- Fluoride is **NOT** contraindicated with levothyroxine

No. 2 LISINOPRIL (generic)

- Antihypertensive Medication Compliance
- Zestril®, Prinivil®
- ACE (Angiotensin Converting Enzyme) inhibitor (ACEi)
- Dental Implications
 - Orthostatic (postural) hypotension-watch out!
 - Scalded mouth syndrome
 - Non-productive cough
 - NSAID interaction with long-term use
 - Angioedema

Other ACE inhibitors

- benazepril (Lotensin®)
- captopril (Capoten®)
- enalapril (Vasotec®, Epaned®)
- fosinopril (Monopril®)
- moexipril (Univasc®)
- pirindopril (Aceon®, Coversyl®)
- quinapril (Accupril®)
- trandolapril (Mavik®)
- Tekturna ® (aliskiren)-direct renin inhibitor

No. 3 ATORVASTATIN (generic)

- HMG-CoA reductase Inhibitor
- Decrease serum total and LDL cholesterol
- grapefruit juice interactions
- Lipitor®
- Similar medications:
 - rosuvastatin (Crestor®)
 - lovastatin (Mevacor®, Altoprev®)
 - simvastatin (Zocor®)
 - pravastatin (Pravachol®)*
 - pitavastatin (Livalo®)
 - fluvastatin (Lescol®)
- possible side effects of statins
 - muscle weakness
 - increased blood glucose or HbA1c
 - decreased cognitive ability-questionable

- CONTRAINDICATED IN PREGNANCY AND BREAST FEEDING

- Do statins influence pulpal morphology?
- New cholesterol lowering medications-expensive
 - PCSK9 inhibitors-mechanism
 - alirocumab (Praluent®) –Sanofi/Regneron
 - evolocumab (Repatha®)-Amgen

No. 4 METFORMIN (generic)

- type II diabetes mellitus
- appoint in the morning
- Glucophage®
- other uses

No. 5 AMLODIPINE BESYLATE (generic)

- calcium channel blocker
- antihypertensive
- gingival hyperplasia
- Norvasc®
- Other calcium channel blockers
 - diltiazem(Cardizem®, Tiazac®)
 - felodipine (Plendil®)
 - nifedipine (Adalat®, Procardia®)
 - verapamil (Covera-HS®, VerelanPM®, Calan)
 - nicardipine (Cardene®)
- clarithromycin interaction-could be fatal

No. 6 METOPROLOL TARTRATE/SUCCINATE (generic)

- Selective Beta Blocking Agent (Beta₁ blocking agent)
- Indications
 - antihypertensive
 - premature atrial (PACs) and/or ventricular contractions (PVCs)
 - other abnormal cardiac rhythms
- Lopressor®, /Toprol XL®
- DO NOT DISCONTINUE ABRUPTLY
- Long-term use of NSAIDs (~ 3 weeks) may diminish hypotensive effectiveness of beta blockers
- Other selective Beta₁ blocking agents
 - nebivolol (Bystolic®)
 - atenolol (Tenormin®)
 - bisoprolol (Zebeta®)
 - acebutolol (Sectral®)
 - esmolol (Brevibloc®)
 - betaxolol (Kerlone®)

No. 7 OMEPRAZOLE (generic)

- hydrogen ion pump inhibitor (PPI)
- GastroEsophageal Reflux Disease (GERD)
- possible side effects related to altered stomach Ph
 - increased risk for hip, wrist, and spine fracture
 - increased risk for Clostridium difficle
 - decreased serum magnesium
 - possible Vitamin B₁₂ deficiency

- similar medications
 - esomeprazole (Nexium®)
 - lansoprazole (Prevacid®)
 - dexlansoprazole (Dexilent®, Kapidex®)
 - rabeprazole (Aciphex®)
 - pantoprazole (Protonix®)
 - Zegarid®-a rapid release form of omeprazole

No. 8 SIMVASTATIN (generic)

- HMG-CoA reductase Inhibitor
- Decrease serum total and LDL cholesterol
- grapefruit juice interactions
- Zocor®

No. 9 LOSARTAN POTASSIUM (generic)

- Angiotensin Receptor Blocker (ARB)
- antihypertensive
- Cozaar®
- Dental Implications
 - Orthostatic hypotension
 - Scalded mouth syndrome
 - Non-productive cough (less than ACE Inhibitors)
 - NSAID interaction with long-term use

No. 10 ALBUTEROL (generic)

- Beta 2 receptor agonist
- bronchodilator
- asthma, COPD
- prevention of exercise-induced bronchospasm
- use caution with aspirin/NSAIDs in some patients
- Ventolin HFA®, Proair HFA®
- ADVAIR DISCUS®
 - fluticasone and salmeterol
 - maintenance treatment of asthma
 - no problems with vasoconstrictor
 - oral candidiasis/aspergillus niger
- *FLUCONAZOLE* (generic)
 - oral antifungal
 - Diflucan®
 - 100 mg BID first day and 100 mg/day for 13 days
 - contraindicated with patients taking clopidogrel (Plavix®)

No. 11 GABAPENTIN (generic)

- Neurontin®
- analgesic for neuropathic pain
 - fibromyalgia
 - diabetic neuropathy
 - post-herpetic neuropathy
- abuse potential?

No. 12 HYDROCHLORTHIAZIDE (generic)

- HCTZ
- diuretic/antihypertensive
- depletes potassium
- eat lots of bananas and drink lots of orange juice
- watch out for potassium chloride supplements

No. 13 HYDROCODONE WITH ACETAMINOPHEN (generic)

- opiate & non-opiate analgesic
- addictive
- second most abused drug by general dentists
- Schedule II (as of-October 6, 2014)
- opiate metabolism-CYP2D6
 - genetic differences
 - NO CODEINE in CHILDREN -see AAP & FDA
- most common side effect of opiates: Nausea and vomiting
- Hydrocodone is more efficacious than codeine as an analgesic but causes less nausea & vomiting
- opiate-induced N/V occurs in CRTZ located in medulla
- analgesic efficacy is not related to N/V
- phenothiazines will block the CRTZ
 - drug interactions between phenothiazines and opiates
 - Rx Hydrocodone with acetaminophen 7.5/325 mg
 Disp. Twelve (12) tablets
 Sig: Take one tablet by mouth every four to six
 hours as needed for the relief of pain.
 Do not exceed six tablets in 24 hours

THE PHARMACOLOGY OF ACETAMINOPHEN

- The analgesic effect of acetaminophen occurs predominantly in the Central Nervous System (CNS)
- Mechanism of action
 - cyclo-oxygenase 3 (COX₃) inhibition
 - located in the central nervous system (CNS)
 - some peripheral effects
- Clinical Effects
 - analgesic
 - antipyretic
 - No gastritis
 - No effects on uric acid-gout☺
 - No anti-platelet effects
 - NO ANTI-INFLAMMATORY EFFECTS
- Maximum daily dose of acetaminophen is 3000 mg
- Maximum effective dose of acetaminophen is 1000 (650) mg

No. 14 SERTRALINE (generic)

- Selective Serotonin Reuptake Inhibitor (SSRI)
- depressive episodes
- chronic fatigue sydrome
- chronic pain
- adjunctive therapy for attention deficit hyperactivity disorder (ADHD)
- Zoloft®
- possible side effects
 - bruxism
 - bleeding

No. 15 AMOXICILLIN (generic)

- Broad spectrum antibiotic
- Antibiotic of choice for most orofacial infections is **penicillin V**

Rx Penicillin V tablets 500 mg Disp: 30 tablets

> Sig: Take two tablets by mouth to start then one tablet every six hours for seven days for infection

- Subacute Bacterial Endocarditis Antibiotic Prophylaxis

Cardiac Conditions Associated with the Highest Risk of Adverse Outcome from Endocarditis for Which Prophylaxis With Dental Procedures is Recommended

- 1. prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts
- 2. prosthetic material used for cardiac valve repair (annuloplasty rings and chords)
- 3. a history of infective endocarditis
- 4. a cardiac transplant with valve regurgitation due to a structurally abnormal valve
- 5. the following congenital (present from birth) heart disease:
 - a. unrepaired congenital cyanotic heart disease, including palliative shunts and conduits
 - b. any repaired congenital heart defect with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or prosthetic device

Antibiotic Prophylaxis for Patients with Orthopedic Prostheses

"The ADA and the American Academy of Orthopaedic Surgeons have found that the evidence does not support routine prescription of antibiotic prophylaxis for joint replacement patients undergoing dental procedures. This finding is based on a collaborative systematic review of the scientific literature." -www.ada.org/news

"In 2014, the ADA Council on Scientific Affairs assembled an expert panel to update and clarify the clinical recommendations found in the 2012 evidence-based guideline, *Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures*. As was found in 2012, the 2014 updated systematic review found no association between dental procedures and prosthetic joint infections. Based on this review, the 2014 Panel concluded that prophylactic antibiotics given prior to dental procedures are *not recommended* for patients with prosthetic joint implants." www.ada.org

www.ada.org member center ADA library and archives	
oral health topics	,

Guest Editorial: ADA Guidance for Utilizing Appropriate Use Criteria in the Management of the Care of Patients with Orthopedic Implants Undergoing Dental Procedures. Journal of American Dental Association-February 2017

www.orthoguidelines.org

"Appropriate Use Criteria"

SBE prophylaxis antibiotics

Rx Amoxicillin tablets 500 mg Disp: 4 tablets

Sig: Take four tablets by mouth 30-60 minutes before dental appointment

Rx Cephalexin tablets 500 mg Disp: 4 tablets

Sig: Take four tablets by mouth 30-60 minutes before dental appointment

- Patients who are allergic to penicillins
 - Rx Clindamycin tablets 150 mg

Disp: 4 tablets

Sig: Take four tablets by mouth 30-60 minutes before dental appointment

Rx Azithromycin tablets 250 mg

Disp: 2 tablets

Sig: Take two tablets by mouth 30-60 minutes before dental appointment

Rx Clarithromycin tablets 250 mg

Disp: 2 tablets

Sig: Take two tablets by mouth 30-60 minutes before dental appointment

SUBSTANCE ABUSE DISORDERS AND THE AMERICAN DENTAL ASSOCIATION

www.ada.org Subs	Advocacystance Use Disorders	Current Policies (6)
V	*****	<***

Statement on Provision of Dental Treatment for Patients with Substance Abuse Disorders

"Dentists are urged to be aware of each patient's substance use history, and to take this into consideration when planning treatment and prescribing medications"

Guidelines Related to Alcohol, Nicotine, and/or Drug Use by Child or Adolescent Patients

Age-related warning signs:

Behavioral changes Health Issues Hygiene/Appearance problems School or work concerns

Statement on Alcohol and Other Substance Use by Pregnant and Postpartum Patients

Prevalence of Fetal Alcohol Syndrome Disorders (FASD)
In the U.S. reported to be 3.1-9.9% (JAMA Feb. 6 2018)
1 in 9 U.S. Women report drinking while
Pregnant MMWR May 2019

I. MARIJUANA

- A. A weed-like plant that has been used a source of food, medicine, as a recreational drug and fiber for clothing since prehistoric times.
 - common street names
 - ganja, sensimilla, giggle smoke, mary jane, dab, scat, shatter, mids
 - the term "dope" rarely used today more contemporary term is "weed"
 - April 20 is considered "Annual Cannabis Day" (the number "420" refers to marijuana)
- B. Identification of cannabis
 - Plant stem will have an odd number of leaves (3, 5, or 7).
 - Each leaf exhibits a serrated edge and the vein pattern is unique
- C. Three Species
 - 1. cannabis sativa
 - plants are tall and sparse (may be up to 20 feet)
 - leaves are long and slender
 - usually grown outdoors
 - ~13 weeks to mature with lower yields
 - more potent than indica species
 - higher concentrations of tetrahydrocannabinol (THC) resulting in more mood changes, perception, behavior, and hallucinations
 - 2. cannabis indica
 - plants are short and compact
 - leaves are broader and short
 - usually grown indoors (shorter growing season)
 - higher levels of cannabidiol (CBD) makes you drowsier than sativa
 - may useful as a sedative, treating epilepsy resistant to traditional medications, relieve pain, muscle spasms and tremors
 - 3. cannabis ruderalis-not significant
- D. Parts of the Plant
 - 1. Seeds, leaves, and stems-low concentration of psychoactive cannabinoids
 - often referred to as "marijuana", "grass", "weed"
 - seeds do not contain any psychoactive cannabinoids-used to grow more plants

- ground up seeds, stems, and leaves are rolled into "joints" or "spliffs"
- as the joint burns down it is referred to as a "roach"
- cigars can be hollowed out and packed with marijuana called "blunts" or "rillos"
- **Hemp** contains less than 0.3% THC
- used to make rope, soaps, cosmetics, clothing, and car parts
- Hemp lollypops can be purchased in shops selling drug paraphernalia
- 2. The "Flowers or "buds"
 - Sex of plant very important-female plant contains higher concentrations of psychoactive chemicals
 - **Sinsemilla** (without seeds)
 - The buds contain hair-like projections called "trichomes"
 - Trichomes contain a resin which is released with heat and pressure-called hashish
 - **Hashish** has the highest concentration of psychoactive cannabinoids
 - = Terpenes-Entourage effects
- E. Chemical composition of cannabis
 - 1. Approximately 483 compounds have been identified 65 have been identified as cannabinoids (active)
 - 2. proportion and type of cannabinoids vary according to species, variety (strain) and growing conditions.
 - 3. strain is named by the grower according to smell, appearance, and psychoactive effects
- F. Clinical pharmacologic effects
 - 1. dose-dependent
 - 2. determined by set and setting of the intoxicated person
 - 3. euphoria (mellowing out) everything becomes \Longrightarrow comical \Longrightarrow problems disappear, munchies \Longrightarrow time and space distortion \Longrightarrow dysphoria \Longrightarrow paranoia, fear, anxiety \Longrightarrow accidental death
 - 4. signs/symptoms of marijuana use
 - a. blood shot eyes
 - b. slow to respond
 - c. slurred speech
 - d. glazed eyes
 - e. odor on breath and clothes

- 5. Excretion/detection
 - a. casual user-2 to 4 days
 - b. heavy user-30 to 60 days
- G. Routes of administration
 - 1. smoked in the form of a cigarette (joint, spliff, etc.)
 - most efficient method
 - quick onset, short duration
 - smoke is dry and harsh
 - water pipe, hookah,"Bong"
 - 2. vaporized in its native state (vegetative material)
 - almost as efficient as smoking without the harsh dry feeling
 - use commercial vaporizers
 - E-cigarettes can be used
 - 3. the cannabinoids can be exacted, concentrated and vaporized
 - butane hash oil (BHO)
 - "dab, "scat", "shatter"
 - "distillates"
 - 4. cannabinoids extracted and incorporated into food such as candy, brownies, cakes, etc.
 - very slow, irregular absorption
 - slow onset, long duration

H. Medical Uses

- 1. Glaucoma
 - need to smoke 6 to 8 times a day-not practical
- 2. Multiple sclerosis-questionable, Scientific research does not support but anecdotally may have some benefit.
- 3. Chronic pain
- 4. Antiemetic-heavy users experience acute hyperemesis
- 5. Hypnotic/Sedative
- 6. Epilepsy
- 7. FDA approved cannabinoid-like synthetics
 - a. approved for anorexia associated with weight loss in patients with AIDS
 - b. To treat nausea and vomiting associated with cancer chemotherapy
 - c. dronabinol (Marinol)-AbbVie, (Syndros)-INSYS
 Therapeutics
 - d. nabilone (Cesamet)-Valeant Pharmaceuticals
 - e. cannabidiol (CBD) (Epidiolex)-GW Pharmaceuticals

I. Impact on the Dental Practice

- 1. Patient
 - a. used by patient to reduce anxiety
 - b. marijuana is a CNS depressant and may amplify oral or IV sedation
 - c. short term memory is impaired. Give written take home instructions
 - d. have witness for consent forms
 - e. heavy 3 or 4 times a week smokers have characteristic stain on teeth

2. Dentist/Staff

- a. psychomotor skills can be impaired for 24 hours after using marijuana
- b. Questions: Should dentists be allowed to use marijuana for medical purposes and continuing practicing?
- c. How do you measure impairment?

3. Family

- a. Is Marijuana addictive-YES. According to the NIDA 9% of marijuana users will become dependent and this increases to 17% when they begin in teen years.
- b. According to NIDA heavy marijuana smokers function at a lower intellectual level compared to non-smokers affecting attention span, memory, cognitive ability, and psychomotor skills

All rights reserved. This material may not be reproduced, published, rewritten, redistributed, or transmitted in whole or part without the express written permission of the author. Any use without the author's consent is prohibited.

©Harold L. Crossley, DDS., M.S., Ph.D.