PHC721 - CLINICAL PROBLEM SET # 5 (Midterm Review)

Patient

Female, 78 years old

Chief Complaint

"A month ago, I lost the filling in my back tooth on the left side. The tooth started hurting last week, so I have been taking **Tylenol**, 650 mg twice a day.

I just saw a commercial that only 400 mg of **Advil**, or as little as 220 mg of **Aleve**, would give the same relief of my pain. Are the other drugs better than Tylenol?

Oh, and you have to be careful, Doc, because I am allergic to the drug you use for numbing. Ten years ago, as soon as this young dentist put the needle in, I could hear my heart pounding, and I was sweating and shaking.

You should know that I am also allergic to painkillers because I had the same reaction when the doctors gave me **Tramadol** after my gallbladder surgery. At that time, I was taking **Prozac** for my depression, but it wasn't strong enough because I wanted to kill myself. This is when my psychiatrist switched my med to **lithium**."

Background and/or Patient History

Atherosclerosis; Bipolar Depression; Congestive Heart Failure; Deep Vein Thrombosis; Essential Hypertension; Liver Cirrhosis; Peptic Ulceration;

Cholecystectomy due to gallstones, 2002; Myocardial Infarction, 2007.

Medications:
Clopidogrel; Hydrochlorothiazide; Labetalol; Lithium; Omeprazole; Rosuvastatin; Warfarin

Current Findings

Extensive endodontic damage: teeth # 19 & 21.

Temp: 98.1 F; BP: 135/95 mmHg; HR: 65 bpm;

BMI: 29

Contingent the outcome of allergy testing, the treatment plan may include local anesthesia with 2% **Lidocaine** and 1:200, 000 **Epinephrine**.

Supplemental Drug Information:

Acetaminophen (Tylenol®), a non-opioid/non-steroidal analgesic and anti-pyretic without anti-inflammatory or anti-platelet effects; unknown mechanisms of action;

Clopidogrel, an anti-platelet agent;

Fluoxetine (Prozac®), a selective serotonin reuptake inhibitor (SSRI) used in the treatment of depression; potent CYP2D6 enzyme inhibitor;

Hydrochlorothiazide, a thiazide diuretic; increases sodium excretion by the kidneys; the efficacy is lowered by NSAIDs;

Ibuprofen (Advil®), a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-pyretic and anti-platelet activities; non-selective COX inhibitor;

Labetalol, a third-generation, non-selective beta-adrenergic antagonist with alpha-1 antagonistic activity;

Lidocaine, a local anesthetic; sodium channel blocker; metabolized in the liver (CYP3A4; hepatic blood flow-limited);

Lithium, the treatment of choice for bipolar disorder; low therapeutic index; excreted unchanged by the kidneys;

Naproxen (Aleve®), a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-pyretic and anti-platelet activities; non-selective COX inhibitor;

Omeprazole, a protein pump inhibitor used in treatment of gastric hyperacidity; the prodrug is activated by CYP2C19 & CYP3A4;

Rosuvastatin, a statin, inhibits the synthesis of cholesterol; excreted primarily through bile;

Tramadol, opioid analgesic, inhibits reuptake of catecholamines, metabolized by CYP2D6 and CYP3A4 to a more active ingredient;

Warfarin, indirectly acting oral anticoagulant; competitively inhibits Vitamin K epoxide reductase; 99% plasma protein-bound.

1. How would you answer the patient's question about the Tylenol vs. Advil vs. Aleve comparison? Is the drug dose more directly related to its potency or efficacy? Would you recommend switching to Ibuprofen or Naproxen because of the smaller drug dose? Which of the patient's medications could lead to dangerous drug interactions with NSAIDs?

2. Please identify all potential PHARMACODYNAMIC interactions between drugs included in the case description (i.e., synergism, functional and receptor-based antagonism). What are their expected effects on drug potency and efficacy?

3. Which drugs are likely to lead to sensitization or PHARMACODYNAMIC tolerance?

4. Please identify all potential PHARMACOKINETIC mechanisms that are likely to modify drug action in this patient, indicating the stage of drug processing and specific parameters being increased or decreased (i.e., Absorption-oral bioavailability; Distribution-volume of distribution; Metabolism & Excretion-elimination half-life):

   A. Pharmacokinetic drug interactions;

   B. Patient factors: Physiological, Psychological, Genetic, and Disease-related;

5. Which drugs are likely to lead to PHARMACOKINETIC tolerance?

6. What steps (if any) should be taken in consideration of the patient's comments about allergy to analgesics and local anesthetics? What are the unique features of drug allergies?

7. Would there be a reason to expect a compromised Rosuvastatin excretion in this patient? Would the patient's health status be likely to compromise the enterohepatic cycling of drugs? What is a common cause of the disruption in drug enterohepatic cycling?