Drug & Poison Information Center—Faculty of Pharmacy—Tanta University

Drug & Poison Information Bulletin

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CDC recommendations for prescribing opioid for chronic pain, 2016

Inside this issue:

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk

for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

Source: www.medscape.com, www.cdc.gov

Fast facts

Fast facts about esophageal cancer

- Risk increases with age.
- < 15% of cases are in people > 55 years.
- 3 to 4 times more common in men than women.

Source: www.medicalnewstoday.com

Fast Facts about colorectal cancer

- Risk increases with age. > 90% of colorectal cancers occur in people aged ≥ 50.
- Precancerous polyps and colorectal cancer don't always cause symptoms, especially at first (Having a screening test is so important).

Symptoms may include:

1. Blood in or on the stool (bowel movement).
2. Stomach pain, aches, or cramps that do not go away.
3. Losing weight without reasons.

Screening test options:

1. Colonoscopy (every 10 years).
2. High-sensitivity fecal occult blood test (FOBT), stool test, or fecal immunochemical test (FIT) (every year).
3. Sigmoidoscopy (every 5 years, with FOBT every 3 years).

Source: www.cdc.gov

A new study proposes for the first time that gum disease bacteria - Porphyromonas gingivalis - could be a risk factor for esophageal cancer

There are two main types of esophageal cancer: esophageal adenocarcinoma and esophageal squamous cell carcinoma (ESCC). ESCC is more common in developing countries. The cancer is hard to diagnose in the early stages. For many patients, the cancer develops rapidly after diagnosis and the prognosis is not good.

The researchers, from the University of Louisville (UofL), KY, and Henan University of Science and Technology in Luoyang, China, tested tissue from 100 patients with ESCC and 30 patients who did not have the disease (the controls).

They tested samples taken from three types of esophageal tissue: cancerous tissue, non-cancerous tissue adjacent to cancerous tissue and normal tissue from the controls.

To detect *P. gingivalis* in the tissue samples, the researchers measured expression of lysine-gingipain, an enzyme unique to the bacterium. They also looked for DNA traces of the bacterial cell.

The researchers found that:

1. *P.gingivalis* was present in 61% of cancerous tissue samples and only 12% of adjacent tissue samples. They found none in the normal tissue samples.

2. They found levels of both the enzyme and the bacterial DNA were significantly higher in the cancerous tissue of than in surrounding tissue or tissue of normal controls.

3. They also found that levels of *P. gingivalis* measures were in line with levels of other measures, such as extent of cancer cell differentiation, metastasis & overall survival rate.

The researchers noted that:

1. These findings provide the first direct evidence that infection could be a novel risk factor for ESCC, and may also serve as a prognostic biomarker for this type of cancer.

2. If these findings are confirmed, then it could mean that eradication of a common oral bacterium could help reduce the significant number of people who develop ESCC.

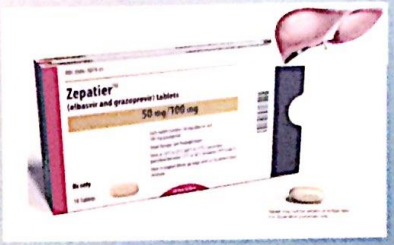
3. It would suggest that improving oral hygiene may reduce ESCC risk; screening for *P. gingivalis* in dental plaque may identify susceptible subjects; and using antibiotics or other antibacterial strategies may prevent ESCC progression.

Source: www.medicalnewstoday.com

Newly Food and Drug Administration (FDA) approved drugs

Zepatier (elbasvir and grazoprevir)

On January 2016 FDA approved ***Zepatier*** which is a fixed-dose combination product containing ***elbasvir***, a hepatitis C virus (HCV) NS5A inhibitor, and ***grazoprevir***, an HCV NS3/4A protease inhibitor.



Zepatier is specifically indicated with or without ribavirin for the treatment of chronic HCV genotypes 1 or 4 infection in adults & supplied as a tablet for oral administration.

Recommended dosage: One tablet taken orally once daily with or without food for 12 or 16 weeks depend on specific genotype and other patient variables.

The FDA approval was based on six studies in 1,373 patients with chronic HCV genotype 1 & 4 infection. The overall sustained virologic response (SVR) ranging from 94 to 97 % in genotype1 infected patients, and 97 to 100 % in genotype 4 infected patients.

Sources: www.centerwatch.com, www.medscape.com

FDA approves first coagulation factor-albumin fusion protein for Hemophilia B

On March 2016 the U.S. FDA approved ***Idelvion***, Coagulation Factor IX (Recombinant), Albumin Fusion Protein, for use in children and adults with Hemophilia B. ***Idelvion*** is the 1st coagulation factor-albumin fusion protein product to be approved, and the 2nd Factor IX fusion protein product approved in the U.S.

Idelvion is used to replace Factor IX that is missing or defective in people with Hemophilia B. ***Idelvion*** is produced by recombinant DNA technology linking Factor IX to albumin, a protein found in blood, which accounts for the product lasting longer when given intravenously. Therefore, it requires less frequent injections than unmodified Factor IX when used for prevention. ***Idelvion is indicated for:***

1. Control and prevention of bleeding episodes.
2. Management of bleeding following surgery (perioperative).
3. As a prophylactic measure to reduce the frequency of bleeding episodes.

Source: www.fda.gov

Pediatric pharmacokinetics refresher for pharmacists

N.B. Pediatric pharmacokinetics affect *drug selection* and *dosing*.

Characteristics expressed in pediatric patients:

Absorption

1. ***Absorption from the GI tract*** is affected by *gastric acid secretion, bile salt formation, gastric emptying time, intestinal motility, bowel length and effective absorptive surface, microbial flora*. All these factors are reduced in neonates (full-term and premature) and all may be reduced or increased in an ill child of any age.

- Reduced gastric acid secretion increases bioavailability of acid-labile drugs (eg, penicillin) and decreases bioavailability of weakly acidic drugs (eg, phenobarbital).
- Reduced bile salt formation decreases bioavailability of lipophilic drugs (eg, diazepam). Reduced gastric emptying and intestinal motility increase the time it takes to reach therapeutic concentrations when enteral drugs are given to infants < 3 mo.
- Drug-metabolizing enzymes present in the intestines of young infants are another cause of reduced drug absorption.
- Infants with congenital atretic bowel or surgically removed bowel or who have jejunal feeding tubes may have specific absorptive defects depending on the length of bowel lost or bypassed and the location of the lost segment.

2. ***IM injections*** are generally avoided in children because of pain and the possibility of tissue damage, but, when needed, water-soluble drugs are best because they do not precipitate at the injection site.

3. ***Transdermal absorption*** may be enhanced in neonates and young infants because the stratum corneum is thin and because the ratio of surface area to weight is much greater than for older children and adults. Skin disruptions (eg, abrasions, eczema, burns) increase absorption in children of any age.

4. ***Transrectal drug therapy*** is generally appropriate only for emergencies when an IV route is not available (eg, use of rectal diazepam for status epilepticus).

Site of placement of the drug within the rectal cavity may influence absorption because of the difference in venous drainage systems. Young infants may also expel the drug before significant absorption has occurred.

5. ***Absorption of drugs from the lungs*** varies less by physiologic parameters and more by reliability of the delivery device and patient or caregiver technique.

Distribution

- The volume of distribution of drugs changes in children with aging due to changes in body composition and plasma protein binding.
- Higher doses (per kg of body weight) of water-soluble drugs are required in younger children because a higher percentage of their body weight is water.
- Lower doses are required to avoid toxicity as children grow older because of the decline in water as a percentage of body weight.
- Many drugs bind to proteins (primarily albumin, α_1-acid glycoprotein, and lipoproteins). Albumin and total protein concentrations are lower in neonates but approach adult levels by 10 to 12 mo. Decreased protein binding in neonates is also due to qualitative differences in binding proteins and to competitive binding by molecules such as bilirubin and free fatty acids, which circulate in higher concentrations in neonates and infants. The net result may be increased free drug concentrations, greater drug availability at receptor sites, and both pharmacologic effects and higher frequency of adverse effects at lower drug concentrations.

Metabolism and elimination

- Drug metabolism and elimination vary with age and depend on the substrate or drug, but most drugs, and most notably phenytoin, barbiturates, analgesics, and cardiac glycosides, have plasma half-lives 2 to 3 times longer in neonates than in adults.
- Kidneys, lungs, and skin also play a role in the metabolism of some drugs, as do intestinal drug-metabolizing enzymes in neonates.
- The cytochrome P-450 (CYP450) enzyme system in the small bowel and liver is the

most important known system for drug metabolism. CYP450 enzymes inactivate drugs via phase I metabolism (oxidation, reduction, and hydrolysis) and phase II metabolism (hydroxylation and conjugation).

- Phase I activity is reduced in neonates, increases progressively during the first 6 mo of life, exceeds adult rates by the first few years for some drugs, slows during adolescence, and usually attains adult rates by late puberty. However, adult rates of metabolism may be achieved for some drugs (eg, barbiturates, phenytoin) 2 to 4 wk postnatally.
- Phase II metabolism varies considerably by substrate.
- Maturation of enzymes responsible for bilirubin and acetaminophen conjugation is delayed; enzymes responsible for morphine conjugation are fully mature even in preterm infants.
- Drug metabolites are eliminated primarily through bile or the kidneys. Renal elimination depends on plasma protein binding, renal blood flow, GFR and tubular secretion. All of these factors are altered in the first 2 yr of life. Renal plasma flow is low at birth (12 mL/min) and reaches adult levels of 140 mL/min by age 1 yr. Similarly, GFR is 2 to 4 mL/min at birth, increases to 8 to 20 mL/min by 2 to 3 days, and reaches adult levels of 120 mL/min by 3 to 5 mo.

Source: www.merckmanuals.com

Editorial board

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