Drug Allergies and Reactions

Michelle Huber PharmD., CGP
Hospice of Siouxland

Objectives

- Differentiate between true allergic response and drug side effects.
- Understand cross-sensitivity between opiates, sulfas, and penicillin drug classes.
- Describe alternative drug choices that can be made with patient allergies.
Drug Sensitivity

- Obtain History
- Sensitivity reactions:

  - Example: Aspirin sensitivity

Pseudoallergy

- Examples: vancomycin and morphine
- Associated with histamine release
Photosensitivity

- Not allergic reaction
- Drug side effect
  - Sulfonamide antibiotics
  - Isotretinoin
  - Tetracyclines

Allergic Cross-Reactivity

- React to drugs with similar chemical structure.
Test your knowledge

- T or F
- Compared to drugs taken orally, drugs that are either injected or applied to the skin are more likely to cause allergic reactions.

Drug allergies

- Obtain history
- Allergic reactions:
Allergic reaction

- Medications can cause many different types of skin reactions. This particular appearance is called a "fixed drug eruption". This type of reaction typically happens in the same location when the person uses the same medication again.

Individual with a rash to ampicillin.
Allergic Reactions

This drug rash was caused by Tegretol. Medications can cause many different skin reactions, with varying rashes.

Test your knowledge

- T or F
- A patient who has experienced an allergy to one drug, is more likely to experience allergic reactions to other drugs.
Obtain Thorough history

- Is there any medicine you cannot take for any reason?
- Why was the medication prescribed?
- How long ago did the reaction occur?
- By what route did you receive the medication?
- What type of reaction occurred?
- When the drug was stopped, what happened?
- Did they treat the reaction with anything?
- Have you taken the medication/similar medication since then? What happened?
- Have you had the same reaction with a different drug?

Test your knowledge

- A patient with sulfa allergies may also react to:
  - A. furosemide
  - B. glyburide
  - C. acetazolamide
  - D. All of the above
Sulfa Allergies: 3 groups

- Sulfonylarylamines
- Non-sulfonylarylamines
- Sulfonamide-moiety containing drugs

Maculopapular rash
Test your knowledge

- You should not use SSD cream in a patient who has an allergy to Bactrim DS?
- True or False

Sulfonylarylamines

- Sulfonylarylamines
- **Antibiotics**
- Sulfadiazine
- Sulfamethoxazole
- Sulfapyridine
- Sulfisoxazole

- Contraindications include ophthalmic (sodium sulfacetamide), topical (silver sulfadiazine [SSD, Silvadene]), and vaginal products (triple sulfa, sulfanilamide)
Non-sulfanylarylaminines

- Acetazolamide (*Diamox*)
- Brinzolamide (*Azopt*)
- Dorzolamide (*Trusopt*) *Warning*
- Methazolamide (*Neptazane*)
- *Warning*
  
  Labeling warns that due to severe reactions to sulfonamides, sensitizations may recur when a sulfonamide is readministered regardless of route of administration.
  
  This warning includes the ophthalmic preparations (brinzolamide and dorzolamide) because they are absorbed systemically.
  
  Two case reports suggest a connection between an anaphylactic reaction with acetazolamide and sulfonamide allergy.

Non-sulfonlyarylaminines

- Celecoxib (*Celebrex*)
- In case reports, celecoxib has been suggested to cross-react with other sulfonamides.
- Risk of cross reactivity between celecoxib and other sulfonamides is not greater than with placebo - (Three meta-analyses evaluations).
Test your knowledge

- Which diuretic is safest to use in a patient with a sulfonamide/sulfa allergy?
  - A. Furosemide
  - B. Indapamide
  - C. Torsemide
  - D. Ethacrynic acid

Non-sulfonylarylamins

- Bumetanide (Bumex)
- Furosemide (Lasix) Precaution
- Torsemide (Demadex) Contraindicated in patients allergic to sulfonyureas
- Some sources recommend that if a diuretic is used in a patient with a history of sulfonamide allergy, the first dose should be reduced and given under medical supervision.
- Bumetanide and furosemide product labeling contain statements that patients may also be allergic to these drugs if they are allergic to sulfonamides.
- Torsemide is contraindicated in patients allergic to sulfonyureas because its chemical structure is a pyridine sulfonylurea.
- Ethacrynic acid does not contain a sulfa group and is a possible alternative in sulfonamide-allergic patients.
Non-sulfonylarylamines

- **Sulfonylureas**
- Chlorpropamide  None
- Glimepiride (*Amaryl*) **Warning**
- Glipizide (*Glucotrol*)  None
- Glyburide (*DiaBeta, others*) **Warning**
- Tolbutamide (*Orinase*)  None
- Tolazamide (*Tolinase*)  None

Non-sulfonylarylamines

- Chlorothiazide (*Diuril*) **Contraindicated**
- Chlorthalidone (*Hygroton*) **Contraindicated**
- Hydrochlorothiazide  **Contraindicated**
- Indapamide (*Lozol*) **Contraindicated**
- Metolazone (*Mykrox,Zaroxolyn*) **Warning**
Non-sulfanylarylamines

- Sulfasalazine (*Azulfidine*) Contraindicated
- Sulfasalazine is broken down in the gut into sulfapyridine and 5-aminosalicylic acid (mesalamine)

Test your knowledge

- T or F
- You can tell by the name of all drugs if they have a sulfa component.
Sulfonamide-moiety

- Naratriptan (*Amerge*)
- Sumatriptan (*Imitrex*)

Test your knowledge

- T or F
- Drugs such as morphine sulfate and potassium bisulfite should not be taken by patients who had an allergic reaction to a sulfonadimide drug.
Sulfa Allergies

- Medications containing Sulfur, sulfites, sulfates
- Example: morphine sulfate
- Sulfite reaction in patients with asthma
- Saccharin
  - Part of tablet excipients
  - Has a sulfonamide moiety

Drugs to avoid in “Sulfa” Allergy
Test your knowledge

- Which is the most commonly reported drug allergy?
- A. sulfa
- B. morphine
- C. penicillin
- D. A and C

Penicillin allergies

- How old were you when the reaction occurred?
- Can you describe the reaction?
- When did the reaction occur? After the first dose? After the tenth dose?
- How was the penicillin administered? Orally? Intravenously?
- Were you taking any other medications at the same time?
- When the penicillin was stopped, what happened?
- Have you since taken a penicillin, cephalosporin, carbapenem, or monobactam?
Types of Penicillin allergic reactions

- Immediate/accelerated or Type I reactions
  - Within 1-72 hrs
  - anaphylactic
- Type II
  - Increased RBC and PLT clearance by lymphoreticular system, hemolysis

Types of Penicillin allergic reactions

- Type III
  - Serum sickness and tissue injury
- Type IV
  - Contact dermatitis
- Idiopathic
  - Maculopapular or morbilliform rash
  - May progress to Stevens-Johnson syndrome
The incidence of cross-reactivity between penicillin and cephalosporins is

- A. 10%
- B. 50%
- C. 25%
- D. < 1%
Cephalosporin Cross Reactivity

- Incidence <1%

Highest Risk

- Penicillin G
- cefoxitin (Mefoxin)
- Amoxicillin
- ampicillin (Omnipen)
- cefaclor (Ceclor)
- cephalexin (Keflex)
- cephradine (Velosef)
- cefprozil (Cefzil)
- cefadroxil (Duricef)
- Cefotaxime (Claforan)
- ceftizoxime (Ceftizox)
- ceftriaxone (Rocephin)
- cefpodoxime (Vantin)
- cefepime (Maxipime)
Carbapenam and Monobactam Cross Reactivity

- Incidence
  - imipenem [Primaxin]
  - meropenem [Merrem]
  - ertapenem [Invanz]
  - doripenem [Doribax]
  - Aztreonam [Azactam]
  - rare

Making medication choices in Penicillin Allergies

- Type I reaction
  - No penicillin
  - No 1st generation cephalosporin
  - May be able to use 2nd, 3rd, or 4th generation cephalosporin-CAUTION
  - No carbopenams or monobactams
    - Skin testing and dose escalation is recommended
Test your knowledge

- Patient allergic to morphine are more likely to experience an allergic reaction to:
  - 1. hydromorphone
  - 2. meperidine
  - 3. methadone
  - 4. oxycodone
  - A. 1 and 2 C. 3 and 4
  - B. 1 and 4 D. 1, 2, and 4

Opiate Allergies and Cross-reactivity

- **Phenylpiperidines**: meperidine *(Demerol)*, fentanyl *(Duragesic, Actiq, Sublimaze)*, sufentanil *(Sufenta)*, remifentanil *(Ultiva)*

- **Diphenylheptanes**: methadone *(Dolophine)*, propoxyphene *(Darvon)*

- **Morphine group**: morphine, codeine, hydrocodone *(Vicodin, Lorcet)*, oxycodone *(Percocet, OxyContin)*, oxymorphone *(Numorphan)*, hydromorphone *(Dilaudid)*, nalbuphine *(Nubain)*, butorphanol *(Stadol)*, levorphanol *(Levo-Dromoran)*, pentazocine *(Talwin)*
Opiate allergies

- Tramadol (*Ultram*)
  - contraindicated in patients with opioid allergy per U.S. and Canadian product labeling. There is not good evidence for cross-sensitivity of tramadol with opioids.
  - However, experts recommend using tramadol only for patients who have mild reactions to opioids.
- Tapentadol (*Nucynta [U.S.]*)
  - does not contain this same contraindication, but the FDA considers tapentadol structurally related to tramadol. Experts also suggest cautious use of tapentadol in patients with opioid allergy.

Types of Reactions to Opiates

- Pseudoallergy
  - Itching
  - Flushing
  - Sweating
  - angioedema
- True allergy
  - Hives, maculopapular rash, erythema multiforme, pustular rash
  - Increased heart rate
  - Low blood pressure
  - Bronchospasm
  - angioedema
Test your knowledge

- Which opiates are most commonly associated with pseudoallergy?
- 1. morphine
- 2. codeine
- 3. meperidine
- 4. oxycodone
- A. 1 and 2  B. 1, 2 and 3
- C. 1, 2, and 4  D. 3 and 4

Pseudoallergy

- Use of a higher potency opioid [Evidence level C; expert opinion].
- Start with a low dose [Evidence level C; expert opinion].18
- Avoid parenteral administration, or slow the administration rate [Evidence level C; expert opinion].2
Pseudoallergy

- Reaction: flushing, itching, sweating, hives, and/or mild hypotension
- Continue opioid
- Add antihistamine
- Dose reduction

- [Evidence level C, expert opinion].

True allergy

- rash, severe hypotension, bronchospasm, angioedema
- Choose opiate in a different structural class
- Monitor patient closely
Fentanyl patch

- Skin reaction directly under patch

Test your knowledge

- These food allergies can be a concern with medications.
  - A. peanuts
  - B. eggs
  - C. soy
  - D. all of the above
  - E. A and B
Food allergies

- Egg allergies
  - FluMist
  - Cleviprex
- Peanut allergies
  - Combivent Inh
  - Atrovent Inh
  - Both contain soy lecithin

References

- PHARMACIST'S LETTER / PRESCRIBER'S LETTER June 2010 – Volume 26 – Number 60601
- PHARMACIST'S LETTER / PRESCRIBER'S LETTER April 2009 – Volume 25 – Number 5015
- PHARMACIST'S LETTER / PRESCRIBER'S LETTER February 2006 – Volume 22 – Number 202
- Rockall CC, Singh M, Block JH. Likelihood and mechanisms of cross-allergenicity between sulfonamide antibiotics and other drugs containing a sulfonamide functional group. Pharmacotherapy 2004;24:566-70.
References

- Executive summary of disease management of drug hypersensitivity: a practice parameter. Joint Task Force on Practice Parameters, the American Academy of Allergy, Asthma and Immunology, the American Academy of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol* 2000;85(Pt 1):565-700.

Questions?