Contrast Agents for Diagnostic Imaging

Presented by
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for PharmCon

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Speaker
Ellen Wilson is a freelance educator based in Greenville, SC. She received a B.S. in Pharmacy and a PhD in Pharmaceutical Sciences from the University of South Carolina. Her pharmacy practice experiences include retail, hospital, and consulting pharmacy. She also has nearly ten years of collegiate teaching experience at both four-year and two-year institutions. Currently, she teaches online pharmacy courses and writes pharmacy continuing education.

Ellen lives in Greenville with her husband, two daughters, one cocker spaniel, and a once-stray cat. She is an active volunteer at both church and school, enjoys gardening and backyard birding, and is trying to master the art of French cooking.

Speaker Disclosure: Dr. Wilson has no actual or potential conflicts of interest in relation to this program.

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CE Credits: 1.0 contact hour

Target Audience: Pharmacists & Nurses

Program Overview:
Most schools of pharmacy do not cover the area of diagnostic imaging to any appreciable extent in the curriculum, so very few practicing pharmacists have a high level of comfort when dealing with issues relating to diagnostic imaging. This program provides an overview of clinically relevant information for the imaging-related medications commonly in use. It reviews the safety improvements in new generations of drugs, risk factors and precautions for the reduction of severe adverse reactions, and the significance of diligent patient screening before contrast exposure and appropriate monitoring after exposure.

Objectives:
• Outline each type of imaging modality – X-ray, MRI, Ultrasound, and Nuclear Medicine
• Describe the pharmaceutical agents used in diagnostic imaging procedures to include safety, contraindications, and adverse events
• Outline the pharmacist’s role in the safe use of contrast agents for diagnostic imaging

How X-Ray Works

• High energy electromagnetic radiation
• Passes through the body to a camera
• X-ray energy is used to make a negative on the film

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How Computed Tomography (CT) Works

- Beam of radiation penetrates the body
- Signal is weakened by skin, fat, muscles, organs, bones
- Detectors send the signal to computers
- Signal is translated into 2D and 3D images

Typical Radiation Doses

Sievert = SI derived unit of dose equivalent radiation

<table>
<thead>
<tr>
<th>Everyday Exposure</th>
<th>Radiation Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watching TV</td>
<td>0.01 mSv/yr</td>
</tr>
<tr>
<td>Roundtrip flight DC-LA</td>
<td>0.05 mSv</td>
</tr>
<tr>
<td>Avg annual exposure in US</td>
<td>3 mSv/yr</td>
</tr>
<tr>
<td>20 cigarettes/day</td>
<td>53 mSv/yr</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Test</th>
<th>Radiation Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray</td>
<td>0.1 mSv</td>
</tr>
<tr>
<td>Dental X-rays</td>
<td>0.4 mSv/yr</td>
</tr>
<tr>
<td>Abdominal CT</td>
<td>10 mSv</td>
</tr>
</tbody>
</table>

IODINATED CONTRAST MEDIA

Terms to Know

Osmolality
- The concentration of dissolved particles/unit of weight
- mOsm/kg \( \text{H}_2\text{O} \)
- Blood = 290 mOsm/kg
- Has direct effect on the tolerability
  - High = poorly tolerated
  - Low/iso = better tolerated
Ionic Low-Osmolality Contrast Media

In the 1960s and 1970s, research began to find agents with lower osmolalities and better tolerance.

ioxaglate, HEXABRIX®

Nonionic Low-Osmolality Contrast Agents

The first of these agents, metrizamide, was introduced in the US in 1978.

metrizamide

Examples of Nonionic LOCM

Iopamidol  Iohexol  Ioversol

Examples of Nonionic LOCM

Iopromide

Ioxilan
Nonionic Iso-Osmolality Dimeric Contrast Agents

**Visipaque**

[iodixanol] injection

320 mg/mL

Safety of Iodinated Contrast Media

<table>
<thead>
<tr>
<th>Adverse Reaction Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historically</td>
</tr>
<tr>
<td>2008</td>
</tr>
</tbody>
</table>

| Serious adverse events | 0.1-0.2% w/IV HOCM |
|                       | 0.01-0.02% w/IV LOCM |

| Fatal outcomes        | 1 in 170,000 injections |

Risk Factors for Adverse Reaction

- Prior reaction*
- Anaphylactic allergies
- Asthma
- Cardiac disease
- Renal insufficiency
- Anxiety (?)

Adverse Reactions from Iodinated Contrast Media

**“Side Effects”**

- Warmth
- Flushing
- Discomfort
- (Pain)

**Mild Reaction**

- Nausea
- Vomiting
- Urticaria
Contrast Agents for Diagnostic Imaging – What Pharmacists Need to Know

Adverse Reactions from Iodinated Contrast Media

<table>
<thead>
<tr>
<th>Moderate Reaction</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Symptomatic urticaria</td>
<td>• Diphenhydramine</td>
</tr>
<tr>
<td>• Vasovagal reactions</td>
<td>• Leg elevation, fluids</td>
</tr>
<tr>
<td>• Mild bronchospasm</td>
<td>□ β-agonist inhaler</td>
</tr>
</tbody>
</table>

Severe Reaction
• Anaphylactoid reaction
• Profound vasovagal reaction, hypotension
• Moderate-severe bronchospasm
• Laryngeal edema
• Seizure
• Pulmonary edema
• Cardiac arrest

Treatment
• Treatment of acute symptoms
• Code

Premedication of At-Risk Patients

<table>
<thead>
<tr>
<th>Steroids</th>
<th>Elective &amp; emergency</th>
<th>diphenhydramine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>IV</td>
<td></td>
</tr>
</tbody>
</table>

Contrast-Induced Nephrotoxicity (CIN)

Information

<table>
<thead>
<tr>
<th>Definition</th>
<th>Incidence</th>
<th>Clinical Course</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>•20-50% rise in Cr</td>
<td>•0.6% w/eGFR &gt;40ml/min</td>
<td>Cr in 24 hrs, peak @ 4 days, normal in 7-10 days</td>
<td>DM and renal insufficiency</td>
</tr>
<tr>
<td>•0.5-2.0mg/dl inc. in Cr</td>
<td>•4.6% @ 40-30ml/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>•Cr inc. of &gt;25%</td>
<td>•7.8% @&lt;30ml/min</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevention of CIN

- **Hydration**—fluids 100ml/hr before and after
- **N-acetylcysteine**—600mg po BID day before and day of contrast injection
- **Prescreen** serum Cr levels in high risk
- **Choice of agent**—LOCM>HOCM
- **Avoid** iodinated contrast media

### Metformin and Iodinated Contrast Media

<table>
<thead>
<tr>
<th>When to hold metformin</th>
<th>Category</th>
<th>Normal renal function</th>
<th>Comorbidities</th>
<th>Hold or monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category I</strong></td>
<td>Normal renal function</td>
<td>No comorbidities</td>
<td>Give</td>
<td></td>
</tr>
<tr>
<td><strong>Category II</strong></td>
<td>Normal renal function</td>
<td>Comorbidities</td>
<td>Hold x48hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Category III</strong></td>
<td>Renal insufficiency</td>
<td>Hold monitor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*American College of Radiology Committee on Drugs and Contrast Media*

### Contraindications of Iodinated Contrast Media

**True contraindications are rare**
- "Not for intrathecal use", "do not use in patient’s with known hypersensitivity"
- Ionic agents not used in myelography

**Some package labeling disputed**
- pheochromocytoma, thyrotoxicosis, dysproteinemias, myasthenia gravis, sickle cell disease

### How MRI Works

- Strong magnetic fields align hydrogen atoms in the body
- Radiofrequency moves the hydrogen atoms out of alignment
- Atoms relax back, releasing energy
- Energy is translated into an image
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GADOLINIUM-BASED CONTRAST MEDIA

Linear GBCM
- Gadopentetate dimeglumine (Magnevist®)
- Gadodiamide (Omniscan®)
- Gadoversetamide (OptiMARK®)

Macro cyclic GBCM
- Gadoteric acid (Dotarem®)
- Gadobutrol (Gadovist®)
- Gadoteridol (ProHance®)
- Gadoxetate disodium (Eovist®)
- Gadofosveset (Ablavar®)
- Gadobenate dimeglumine (MultiHance®)
Safety of GBCM for MRI
When given at 0.1-0.2 mmol/kg

<table>
<thead>
<tr>
<th>Adverse Reaction Rate</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild reactions</td>
<td>0.07-2.4%</td>
</tr>
<tr>
<td>Injection site rxn, N/V, headache, paresthesias, dizziness, itching</td>
<td></td>
</tr>
<tr>
<td>Allergic-type</td>
<td>0.004-0.7%</td>
</tr>
<tr>
<td>Rash, hives, bronchospasm (rare)</td>
<td></td>
</tr>
<tr>
<td>Anaphylactoid</td>
<td>0.001-0.01%</td>
</tr>
<tr>
<td>Fatal outcomes</td>
<td>Extremely rare</td>
</tr>
</tbody>
</table>

Risk Factors for Adverse Reaction

- X8
- ~4%
  - previous reaction
  - asthma
  - allergies

Patients with risk factors should be pre-medicated

GBCM and Nephrotoxicity

GBCM are NOT nephrotoxic at usual doses

MRI/GBCM may be used in place of CT w/contrast for patients at risk of CIN

GBCM be used in place of iodinated contrast media for CT and angiographs

Nephrogenic Systemic Fibrosis (NSF)

A
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GBCM Structure and NSF

<table>
<thead>
<tr>
<th>GBCM</th>
<th>Doses (millions)</th>
<th># of NSF cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>gadodiamide (Omniscan®)</td>
<td>13</td>
<td>382</td>
</tr>
<tr>
<td>gadopentetate dimeglumine (Magnevist®)</td>
<td>23</td>
<td>195</td>
</tr>
<tr>
<td>gadoversetamide (OptiMARK®)</td>
<td>4.7</td>
<td>35</td>
</tr>
</tbody>
</table>

GBCM associated with few cases of NSF

gadobenate (MultiHance®), gadoteridol (ProHance®)
gadoteric acid (Dotarem®), gadobutrol (Gadavist®)

Incidence of NSF by GBCM

American College of Radiology Committee on Drugs and Contrast Media

Prevention of NSF

peritoneal HD > HD = AKI > CKD(5) > CKD(4)

- Avoid GBCM
- Lowest possible dose
- Hold EPO and FE
- Correct serum Ca²⁺/PO₄³⁻

Contraindications of GBCM for MRI

- None, none known
- Patients with known allergic or hypersensitivity reactions to gadolinium-based contrast agents
  - Omniscan®, MAGNEVIST®, OptiMARK®,

- Chronic, severe kidney disease (GFR < 30 mL/min/1.73m²) or acute kidney injury
How Ultrasound Works

- Transducer delivers short pulses of high frequency sound waves
- Echos are detected
- Different tissues create different echoes
- Pregnancy, soft tissues, heart (ECHO)

Acoustic Impedance Values

<table>
<thead>
<tr>
<th>Material</th>
<th>Impedance (gm/cm² sec x 10⁻⁵)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>0.0004</td>
</tr>
<tr>
<td>Fat</td>
<td>1.38</td>
</tr>
<tr>
<td>Water (50°C)</td>
<td>1.54</td>
</tr>
<tr>
<td>Brain</td>
<td>1.58</td>
</tr>
<tr>
<td>Blood</td>
<td>1.61</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.62</td>
</tr>
<tr>
<td>Liver</td>
<td>1.65</td>
</tr>
<tr>
<td>Muscle</td>
<td>1.70</td>
</tr>
<tr>
<td>Bone</td>
<td>7.80</td>
</tr>
</tbody>
</table>

Ways to Enhance Ultrasound

Safety of Perflutren-Based Contrast Agents

<table>
<thead>
<tr>
<th>Event</th>
<th>Occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious cardiopulmonary reactions</td>
<td>Uncommon usually w/in 30 mins of administration</td>
</tr>
<tr>
<td>Anaphylactoid</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>
Contraindications of Perfluorhexane-Based Contrast Agents

<table>
<thead>
<tr>
<th>OPTISON® &amp; DEFINITY®</th>
<th>OPTISON®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not administer to patients with known or suspected:</td>
<td></td>
</tr>
<tr>
<td>Right-to-left, bi-directional, or transient right-to-left cardiac shunts</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity to perfluorhexane</td>
<td></td>
</tr>
<tr>
<td>Do not administer by intra-arterial injection</td>
<td></td>
</tr>
</tbody>
</table>

Do not administer to patients with hypersensitivity to blood, blood products, or albumin.

Types of Radiation α, β, γ and positron emission

<table>
<thead>
<tr>
<th>Type</th>
<th>Emission</th>
<th>Penetrating Power</th>
<th>Ionizing Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>α</td>
<td>2 protons 2 neutrons</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>β</td>
<td>N→P⁺+e⁻</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>γ</td>
<td>Electromagnetic radiation</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>positron</td>
<td>positron</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

NUCLEAR MEDICINE
WHAT MAKES AN ATOM RADIOACTIVE?

WHAT IS POSITRON EMISSION TOMOGRAPHY (PET)?
- Radiotracer given to the patient
- Energy is emitted from the body
- The PET scanner detects the energy
- Translates into a 3D image
- PET-CT superimposes an anatomical image
Isotopes of Iodine

<table>
<thead>
<tr>
<th>Emission</th>
<th>Products</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>131 β</td>
<td>HICON® &amp; generics caps and soln</td>
<td>Hyperthyroid &amp; carcinoma</td>
</tr>
<tr>
<td>t₁/₂=8 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>123 γ</td>
<td>AndreView® (iofenguane IV)</td>
<td>Diagnostic for pheochromocytoma &amp; neuroblastoma</td>
</tr>
<tr>
<td>t₁/₂=13.2 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>125 γ</td>
<td>Sodium I-123 oral dose</td>
<td>Thyroid diagnostic procedures</td>
</tr>
<tr>
<td>t₁/₂=60 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>125 γ</td>
<td>BrachySource®</td>
<td>Used in long-term brachytherapy</td>
</tr>
</tbody>
</table>
Adverse Reactions and Contraindications to Radiopharmaceuticals

**ADVERSE REACTIONS**
- Hypersensitivity
- N/V, rash, pruritis, hives, injection site rxn
- Angina, HTN, flushing
- Neck tenderness, swelling, pain after thyroid treatment (I-131)

**CONTRAINDICATIONS**
- Previous anaphylactoid reaction
- Murine sensitivity (NeutroSpec®)
- Pregnancy/Nursing (suspend)

Post-Procedure Precautions
*For the first 12 hours*
- Toilets not urinals, repeated flushes
- Wash soiled clothes separately, store x1-2 wks
- Increase intake of fluids to promote elimination
- Sleep alone, no close contact or intimacy
- Wash sink/tub, use separate linens, wash clothes separately
- Avoid handling personal hygiene items of others

The Role of the Pharmacist
*The Joint Commission*

**2004 TJC**
- "Legend drugs" to include contrast media, radiopharmaceuticals
- Must be prepared under direct supervision by RPh, MD, OD

**HHS Code of Federal Regulations**
- Recent TJC citations include
  - Contrast agent storage
  - Lack of labeling
  - Inability to provide orders
  - Lack of monitoring of emergency medical supplies
  - Radiopharmaceutical prepared by technologists
What Can YOU Do?

• Explain procedures
• Discuss normal side effects
• Discuss adverse reactions
• Talk about premedication regimens
• Counsel metformin patients
• Radioisotope precautions

Notes

Notes