Pharmacy Practice Pearls

Clinical Impact of a Pharmacist in Discharge Medication Reconciliation

Teresa Chu, PharmD
Swedish Covenant Hospital
Chicago, Illinois

Objectives

1) Describe the clinical role of a pharmacist performing discharge medication reconciliation.

2) Explain the impact a pharmacist can have on readmission rates with medication reconciliation, clinical, and prescription-related interventions.

**I have no potential/actual conflict of interest to declare**

Medication Reconciliation

- Reconcile medication profiles from each transition of care (i.e., home → inpatient → discharge).
  - (61% incomplete med hx on admission, 33% discharged pts with med-related problems)
- Provide the patient an updated medication list.
- Counsel the patient on new and continued home medications.
- Check prescriptions to ensure all legal requirements are met.

Going Beyond Med Recon.

- At discharge, go beyond medication reconciliation and prescription-interventions
- Take steps toward making clinical-interventions:
  - Maintain open communications with prescribers
  - Maintain open communications with nurses
  - Update ourselves on current treatment guidelines

Clinical Interventions

1) Review the patient’s chief complaint and the resolution of acute issues.

2) Evaluate the continuum of care patient received from one level of triage to another, including the discharge plan

3) Intervene when prescribed discharge medication regimen is suboptimal according to evidence-based recommendation standards.

Clinical Interventions (cont.)

| Are the discharge medications prescribed appropriate? | Match the drug with patient’s problem list. |
| Are continued home medications appropriate? | Prescribing should be evidence-based. |
| Are prophylactic drugs included? | |
| Are all medications at optimal/target doses? | Medications should be dosed according to the most current treatment guidelines. |
| 52.2% of discharge medication profiles require dose adjustments² | |

²Includes dose errors due to omission, incorrect dosage, or interval errors.
Clinical Interventions (cont.)

- Recommend to discontinue medications without appropriate indications.
- Recommend to add omitted medications if indicated.
- 20% of discharge medication profiles require the discontinuation or addition of medication(s).

Impact of a D/C Pharmacist

- PHARMACISTS can potentially increase medication compliance and reduce adverse drug events.3
- PHARMACISTS may impact readmission rates.4
- Quality-of-care improvement
- Cost-saving interventions (stream-lining to less expensive therapy, d/c unnecessary meds, route modifications) can lower drug cost by 41%.5

Zadeh MD, Chu T. Impact of Pharmacist Discharge Counseling on Medication Adherence and Hospital Readmission Rates Swedish Covenant Hospital

- A prospective, randomized study; currently in progress
  Primary Objective: To evaluate whether discharge medication reconciliation and counseling by pharmacists can increase a patient’s medication adherence and reduce hospital readmission rates
  Secondary Objective: To assess and compare the patient’s medication adherence 1-2 weeks vs. 30-45 days post-discharge

Inclusion Criteria: New onset or history of CHF and/or COPD
Exclusion Criteria: Not being discharged home, pre-planned hospital readmission

References

Pharmacy Practice Pearls

Clinical Impact of a Pharmacist in Discharge Medication Reconciliation
Teresa Chu, PharmD
0121-0000-14-018-L04-P

Learning Assessment Questions:

1. All of the following are procedures involved in the medication reconciliation process, except:
   a. Communicating with the physician when a dosing regimen is suboptimal or not indicated.
   b. Including herbal and homeopathic medications as part of the home medication history for reconciliation.
   c. Reconciliation of the patient’s home medications and discharge medications is sufficient.
   d. Recommending prophylactic drugs to the physician for long-term disease state management during discharge.

2. All of the following results can be objectively measured when a pharmacist is included in the reconciliation process, except:
   a. Improvement in quality-of-care
   b. Lowering readmission rates
   c. Lowering drug costs
   d. Reduction of adverse drug events
Pharmacy Practice Pearls

Innovative Use of Integrated Technology to Prevent Human Error in Providing Medications from the Point of Prescription to the Patient’s Bedside

Alicia Juska, PharmD, BCPS
Swedish Covenant Hospital
Chicago, IL

Conflict of Interest Disclosure

• Alicia Juska, the speaker, has no actual or potential conflict of interest in relation to this presentation.

Objectives

• Explain how integration of robotics, automation, and technology can reduce potential medication errors for patient specific drug selection, packaging, dispensing, and administration of bar coded unit doses.
• Identify ways that implementation of a centralized medication storage and dispensing robot with pass through access to the clean room can reinforce compliance with Chapter 797 guidelines and improve the environment for compounded sterile products (CSPs).

Medication Error Data

• Medication errors are 1 of the 6 leading avoidable costs in U.S. health care1
  – Avoidable cost opportunity from medication errors is $20 billion (range $15-28 billion)1
• 450,000 adverse drug events occur annually2
  – 25% of these medication errors are preventable2
• Technology has been introduced to improve accuracy of the medication use system2

National Data for Use of Technology in Hospitals

• 30% use computerized provider order entry3
• 50% use barcoded medication administration3
• 65% of clean rooms were compliant with Chapter 797 guidelines for CSPs4
• 11% use robots4
• 18% use carousels4

How many of you currently use the following in your inpatient pharmacy?

A. Computerized Prescriber Order Entry (CPOE)
B. Bedside Medication Verification (BMV)
C. Electronic Medication Administration Record (EMAR)
D. Robotics (Boxpicker, Carousel, etc)
Swedish Covenant Hospital

- **Overview**
  - 300 bed hospital on the Northwest Side of Chicago
  - Community, non-profit, independent, teaching hospital
  - Decentralized pharmacy model with one central pharmacist to oversee distribution

- **Technology (at SCH in 2012)**
  - Pharmacy redesign and robotic installation
  - CPOE, EMAR, and EHR in place
  - BMV in progress

Remodeled SCH Inpatient Pharmacy

- **Overview with Centralized Med Storage & Dispensing Robot**

System-wide National Drug Code (NDC) Linked Barcode Technology

- From computerized prescriber order entry (CPOE)
- To pharmacist order verification
- To dispensing a unit dose
  - 10% from a centralized medication storage and dispensing robot or
  - 90% via decentralized automated dispensing cabinets (ADCs)
- To bedside medication verification (BMV) with electronic charting on the medication administration record (EMAR)

Medication Use System Control

- All medications must be barcoded when received from the wholesaler
  - New NDCs (change in manufacturer, backorder item replacement) must be entered in the system
- All medications must be assigned an NDC linked barcode prior to being filled in the:
  - Centralized medication storage and dispensing robot
  - Unit dose packager
  - Decentralized ADCs
- Above steps ensure a nurse will be able to scan the medication on the floor

Barcoded Unit Dose

- From Robot
- From Prepackaging Machine
How many times does a technological double check (barcode scan) occur prior to a dose being administered to a patient at bedside?

A. 2
B. 4
C. 6
D. 8

Barcode Scan Throughout the Medication Use System

- Filling robot with daily shipment received
- When removing and/or refilling robot with barcoded unit doses made by the automated prepacking machine
- When removing a dose from the robot an individual label with a barcode is printed
- Prior to any ADC refill
- When the nurse removes a dose from the ADC
- During BMV, prior to patient administration, and for concurrent EMAR documentation

Benefits of Technological “Double-Checks” Using System-wide Barcodes

- Prevent human errors and decrease medication errors
- Reinforce appropriate preparation of unit doses
- Increase level of accurate dispensing of unit doses for both oral and intravenous medications and restocking of ADCs
- Decrease number of missing doses
- Streamline pharmacy workflow
- Tighten control of pharmacy inventory for both oral and injectable medications
- Free pharmacists’ time from dispensing duties to allow for more clinical patient-care activities
- Future “tech check tech” possibilities
- Increase patient safety

Changing Gears and On to the IV Side

Aseptic Garbing, Hand Washing, Gowning, and Gloving Practices of Compounding Personnel

- To enter, compound, and leave the IV room correctly takes 21 steps
- Highlights include:
  - Putting on shoe covers one at a time, crossing into the clean ante-area of the IV room
  - Putting on a head cover, beard mask, face mask
  - Hand washing and drying
  - Gowning
  - Collecting compounding items (drugs, needles, syringes)
  - Disinfecting hands with a waterless, alcohol-based surgical hand scrub
  - Gloving

What is the most appropriate process for entering the IV room?

A. gown, shoe covers, wash hands, gloves, hair cover, alcohol-based surgical hand scrub
B. shoe covers, wash hands, gloves, gown, hair cover, alcohol-based surgical hand scrub
C. hair cover, gown, shoe covers, wash hands, gloves, alcohol-based surgical hand scrub
D. shoe covers, hair cover, wash hands, gown, alcohol-based surgical hand scrub, gloves
Chapter 797 Environmental Control Requirements\textsuperscript{5,6}

- Designated, separate, well-light area
- 68\textdegree F or cooler
- Relative humidity 30-60%
- HEPA filtered air
  - Unidirectional flow
  - Sufficient velocity to sweep particles away from compounding area
  - Introduced at ceiling with returns mounted low on the walls

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Chapter 797 Recommended Action Levels for Microbial Contamination\textsuperscript{5,6}

<table>
<thead>
<tr>
<th>ISO Class</th>
<th>Surface Sample (Contact Plate) (cfu per plate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>7</td>
<td>&gt; 5</td>
</tr>
<tr>
<td>5</td>
<td>&gt; 3</td>
</tr>
</tbody>
</table>

Surface sampling to be conducted every 6 months

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Clean Room Pre-Remodel

- Ceiling with Dust Pockets
- Cooling and Air Filtration System

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Remodeled Clean Room

Sealed Ceiling Tiles and Floor Molding, HEPA Filters in Ceiling, Low Vent Returns, Closed Door to Direct Compounding Area

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Clean Air Room Access Comparison

- Door of Ante Room Leading into Buffer Room Entrance (Full garbing)
- Pass Through Window (No garbing)
Pass Through Window

- Advantages
  - Decrease traffic in and out of IV room
  - Personnel
  - Carts (wheeled through pharmacy past front door)
- Save personnel time to garb
- Decrease $ spent on garbing/gowning supplies to enter IV room
- Pharmacist can check stat medication quickly

Compounding Supplies Pre-Remodel

IV Room Supplies in Pharmacy Storage Area

Supplies in Ante Room

Remodeled Compounding Supplies

IV Room View

Supplies in Ante Room

Pharmacy Automation

Inside Centralized Med Storage (Drug Bins & Robot)

Med Pick Station

Robot & Refrigerated Compartment

Inside Centralized Med Storage

Additional Med Pick Station

in IV Room

- Advantages
  - Allows IV technician access to IV medications without leaving IV room
  - Room temperature medications AND Refrigerated medications
  - Improves workflow and technician efficiency
  - Requires technician to barcode scan each drug removed for compounding
  - Maintains inventory count for IV medications without requiring entry of buyer into the IV room
References

1. Avoidable costs in U.S. healthcare, the $200 billion opportunity from using medicines more responsibly, IMS Institute for Health Informatics. 2013:20-22.
Pharmacy Practice Pearls:
Innovative Use of Integrated Technology to Prevent Human Error in Providing Medications from the Point of Prescription to the Patient’s Bedside
Alicia Juska, Pharm D, BCPS
0121-0000-14-018-L04-P

Learning Assessment Questions

Choose the best answer:

1. What is the benefit of using a barcoded medication administration system?
   A. Print a report for drug recalls on a specific lot of a drug given to a patient
   B. Intercept potential medication errors prior to patient administration
   C. Start allowing technicians to check technician prepared doses to send to floors
   D. Save time on restocking shelves when drugs are received from the wholesaler

2. According to the USP Chapter 797 guidelines, what is the recommended action level for surface sample microbial contamination of the laminar airflow workbench?
   A. Greater than 100
   B. Greater than 10
   C. Greater than 5
   D. Greater than 3
Pharmacy Practice Pearls

Drug Choice and Dosing in the Patient with Advanced Liver Disease

Mia Schmiedeskamp-Rahe
PharmD, PhD, BCPS

There are no conflicts of interest to declare

Objectives

• Identify patients with advanced liver disease requiring dose adjustments of medications.

• Discuss the principles of selecting medications appropriate for patients with advanced liver disease.

The problem

• Liver disease is 12th leading cause of death
• 5th leading cause in 45-64 year olds

• Studies often omit severe liver disease
• Little information in disease-state guidelines
• Little information in package inserts

The goal

• Recognize patients with advanced liver disease

• Account for advanced liver disease
  – When selecting medications
  – When dosing medications

Identifying patients with advanced liver disease

• Patients with cirrhosis that is decompensated
  – presence of jaundice
  – ascites
  – hepatic encephalopathy
  – large esophageal or gastric varices

• Patients with Child-Pugh class B or C cirrhosis
### The Child-Pugh score

<table>
<thead>
<tr>
<th>Attribute</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>&lt; 2</td>
<td>2 – 3</td>
<td>&gt; 3</td>
</tr>
<tr>
<td>INR</td>
<td>&lt; 1.7</td>
<td>1.7 – 2.3</td>
<td>&gt; 2.3</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>&gt; 3.5</td>
<td>2.8 – 3.5</td>
<td>&lt; 2.8</td>
</tr>
<tr>
<td>Ascites</td>
<td>none</td>
<td>controlled</td>
<td>refractory</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>none</td>
<td>mild</td>
<td>poorly controlled</td>
</tr>
</tbody>
</table>

Applicable to those with cirrhosis  
Score ranges from 5 to 15

### Points Class 1 - year survival  2 - year survival

- **5 - 6**  
  - Class A  
  - 1-year survival: 100%  
  - 2-year survival: 85%
- **7 - 9**  
  - Class B  
  - 1-year survival: 81%  
  - 2-year survival: 57%
- **10-15**  
  - Class C  
  - 1-year survival: 45%  
  - 2-year survival: 35%

Patients with class B and C cirrhosis  
have advanced (decompensated) liver disease

### Patient case #1

- A patient diagnosed with cirrhosis has the following:  
  - No ascites  
  - No hepatic encephalopathy  
  - INR = 2.0  
  - Tbil = 1.1 mg/dl  
  - Albumin = 2.0 g/dl  
  - Large esophageal varices

- Does this patient have advanced liver disease?

Child-Pugh score is 8 and class is B: advanced liver disease  
The large varices also indicate decompensated liver disease

### Patient case #2

- A patient diagnosed with cirrhosis is starting interferon, ribavirin and sofosbuvir for hepatitis C.  
  - No ascites  
  - No hepatic encephalopathy  
  - INR = 1.3  
  - Tbil = 0.9 mg/dl  
  - Albumin = 3.8 g/dl  
  - No varices

- Does this patient have advanced liver disease?

Child-Pugh score is 5 and class is A, with no signs of decompensation: this is not advanced liver disease
Strategy for choosing drugs in advanced liver disease

• Several recent articles delineate concerns and underlying principles

• Strategy should be systematic and straightforward

• Should be usable by general practitioners

Step #1: Avoid hepatotoxins

• Consider if the drug has a well-established risk of liver failure

• livertox.nih.gov is a helpful resource

Examples:

– Avoid isoniazid in favor of a fluoroquinolone
– Avoid phenytoin, carbamazepine in favor of levetiracetam
– Avoid darunavir in favor of other options for HIV

Step #2: Avoid nephrotoxins

• Advanced liver disease predisposes to renal failure

• Avoid medications with high nephrotoxic potential

• Examples:
  – Avoid NSAIDS
  – Avoid aminoglycosides unless only option
  – Monitor vancomycin to avoid supra-therapeutic levels
  – Expect that contrast dye will precipitate renal failure

Step #3: Determine if drug will accumulate

• Drugs metabolized in the liver will accumulate
  – Oxidation is more affected
  – Conjugation is less affected
  – In the most advanced cases this distinction is less prominent

• These patients often have brittle renal function
  – Those who regularly experience acute kidney injury are at risk to accumulate renally-cleared drugs
  – Example: avoid glyburide in favor of glipizide

Step #4: If drug accumulates, can this be monitored?

• If the drug is expected to accumulate, this can be managed by therapeutic drug monitoring

• Examples:
  – Warfarin
  – Tacrolimus and cyclosporine
  – Antiarrhythmics

Step #5: Will unmonitored accumulation present a risk?

• If side effects of undetected high levels are unacceptably dangerous, best to avoid

• Examples would include arrhythmias, seizures, bleeding
  – high-dose tricyclic antidepressants
  – bupropion
  – dipyridamole
Step #6: Is the drug likely to worsen encephalopathy?

- Many drugs precipitate hepatic encephalopathy

- Examples:
  - Avoid benzodiazepines except when absolutely necessary
  - Avoid hypnotic drugs like zolpidem, eszopiclone
  - Avoid opioids if a less-sedating drug works (e.g. tramadol, < 2 g/day acetaminophen)
  - Minimize other sedating drugs such as TCA for neuropathic pain

Choosing doses with package insert

- Package inserts may offer guidance
- Usually based on Child-Pugh score

- Example: Tigecycline
  - Mild to moderate hepatic impairment (Child-Pugh class A or B): No dosage adjustment necessary
  - Severe hepatic impairment (Child-Pugh class C):
    Initial: 100 mg single dose; Maintenance: 25 mg every 12 hours

Strategy for choosing doses without guidance from package insert

- Examples: glipizide XL, propranolol
  - No dose recommendations for hepatic impairment in manufacturer’s labeling

- Strategy: Start low and go slow
  - Start at or near lowest available dose
  - titrate slowly
  - monitor parameters that can reveal accumulation

Patient case #3

- A cirrhotic patient with ascites, large varices, hepatic encephalopathy and INR = 3.0 is newly started on the following drugs:
  - isoniazid for treatment of latent tuberculosis
  - ibuprofen for mild back pain
  - bupropion for smoking cessation
  - lorazepam for anxiety
  - propranolol 20 mg bid for varices

Which one of the newly started drugs is most appropriate for this patient with advanced liver disease?

A. Isoniazid
B. Ibuprofen
C. Bupropion
D. Lorazepam
E. Propranolol

Questions?
Reading list

Pharmacy Practice Pearls:
Drug Choice and Dosing in the Patient with Advanced Liver Disease
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0121-0000-14-018-L04-P

Learning Assessment Questions

1. For a patient with chronic liver disease due to hepatitis C, which finding would be sufficient to indicate decompensated liver disease?
   A. Cirrhosis on liver biopsy
   B. Serum albumin 3.0 g/dl
   C. Refractory ascites
   D. Total bilirubin 2.2 mg/dl

2. A 55 year-old patient with Child-Pugh class C liver disease (weight 60 kg, serum creatinine 0.8 mg/dl) is prescribed medications for hospital discharge, including furosemide 40 mg po daily, spironolactone 50 mg po daily, levetiracetam 500 mg po q12h, propranolol 20 mg po q12h and ibuprofen 400 mg po q6h prn mild pain.

Which medication should be challenged by the clinical pharmacist on the basis it should not be used in patients with severe liver disease?

A. Spironolactone
B. Levetiracetam
C. Propranolol
D. Ibuprofen
Pharmacy Practice Pearls

Colistin Dosing: A Literature Review

By:
Kanan Shah, Pharm.D.
Hee Jung Kang, Pharm.D., BCPS

Conflict of Interest Declaration

Authors have no actual or potential conflict of interest in relation to this activity

Learning Objectives

- Discuss the risks and benefits of the different dosing strategies available in the current literature.
- Explain colistin’s role in combination regimens for multidrug resistant gram negative infections.

Colistin: The Basics

- Colistin methanesulfonate (CMS) IV form
- CMS inactive prodrug for colistin base (CBA)
- Polymyxin E
- Bactericidal
  - disrupts outer cell membrane → intracellular component leakage → cell death
- Last-line treatment of multi-drug resistant gram negative bacteria

Colistin Potency

- 1 IU of colistin = amount of colistin that inhibits growth of Escherichia coli 95 I.S.M. in 1 ml broth of pH 7.2
- 1 mg colistin base activity (CBA) = 2.4 mg CMS
- 12,500 IU = 1 mg CMS
- 30,000 IU = 1 mg CBA

What is the dose of colistin in CBA that corresponds to 9 million IU of colistin?

A. 100 mg  
B. 150 mg  
C. 300 mg  
D. 720 mg

Falagas ME. Use of international units when dosing colistin will help decrease confusion related to various formulations of the drug around the world. Antimicrob Agents Chemother. 2006;50(3):2274-2275.
**Manufacturer Recommended Dosing**

**USA Colistimethate (expressed in mg CBA)**

<table>
<thead>
<tr>
<th>Normal Renal Function</th>
<th>Mild Renal Impairment</th>
<th>Moderate Renal Impairment</th>
<th>Considerable Renal Impairment</th>
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</thead>
<tbody>
<tr>
<td>Plasma Creatinine (mg/dL)</td>
<td>0.7 – 1.2</td>
<td>1.3 – 1.5</td>
<td>1.6 – 2.5</td>
</tr>
<tr>
<td>Urea Clearance (L/min)</td>
<td>80 – 100</td>
<td>40 – 70</td>
<td>25 – 40</td>
</tr>
<tr>
<td>Unit Dose CMS (mg)</td>
<td>100 - 150</td>
<td>75 - 155</td>
<td>66 - 150</td>
</tr>
<tr>
<td>Frequency (times/day)</td>
<td>4 - 2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total Daily Dose (mg)</td>
<td>100</td>
<td>150 - 230</td>
<td>133 - 150</td>
</tr>
<tr>
<td>Approximate Daily Dose (mg/kg/day)</td>
<td>5</td>
<td>2.5 - 3.8</td>
<td>2.5</td>
</tr>
</tbody>
</table>


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**Dosing Strategies**

- **Direct Intermittent Administration**
  - Half daily dose over 3-5 minutes every 12 hours

- **Continuous Infusion**
  - Half daily dose over 3-5 minutes
  - After 1-2 hours administer remaining daily dose over 22-23 hours


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**Resistance Breakpoints**

<table>
<thead>
<tr>
<th></th>
<th>CLSI</th>
<th>EUCLAST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinobacter spp.</td>
<td>≥4 mg/L</td>
<td>&gt;2 mg/L</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>≥8 mg/L</td>
<td>&gt;4 mg/L</td>
</tr>
</tbody>
</table>

*Clinical and Laboratory Standards Institute ** European Committee on Antimicrobial Susceptibility Testing

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**Plachouras et al.**

- **Dosing regimen**
  - 100 mg CBA Q8H if CrCl ≥ 50
  - 67mg CBA Q8H if CrCl < 50
- Modeled serum colistin levels based on PK data from 18 subjects


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**Plachouras et al.**

<table>
<thead>
<tr>
<th>Dosing Strategy</th>
<th>Time to Reach Peak</th>
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<tbody>
<tr>
<td>150 mg (15 min infusion) Q8H</td>
<td>&gt;36 hrs</td>
</tr>
<tr>
<td>300 mg (15 min or 2 hr infusion) X1 dose then 150 mg (15 min infusion) Q12H</td>
<td>&gt;12 hrs</td>
</tr>
<tr>
<td>450 mg (15 min or 2 hr infusion) X1 dose then 150 mg (15 min infusion) Q12H</td>
<td>&lt;12 hrs</td>
</tr>
</tbody>
</table>


**Garonzik et al.**

- Open-label population PK study in critically ill patients
- n=105
- 851 serum samples
- 12 patients on HD
- 4 patients on CRRT

**Dose**

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Dose calculation1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading</td>
<td>CBA (mg) = colistin $C_{ss,avg}$ target x 2 x body wt (kg) Max: 300 mg CBA</td>
</tr>
<tr>
<td>Maintenance Dose</td>
<td>Daily dose CBA (mg) = colistin $C_{ss,avg}$ target x (CrCl / 75) Max: 300 mg CBA</td>
</tr>
<tr>
<td>Intermittent HD</td>
<td>Daily dose CBA (mg) = colistin $C_{ss,avg}$ target x 30 Supplemental dose: Add 50% daily dose if admin last hour of HD OR 30% daily dose if admin after HD</td>
</tr>
<tr>
<td>CBT</td>
<td>Daily dose CBA (mg) = colistin $C_{ss,avg}$ target x 150</td>
</tr>
</tbody>
</table>

1. Administer 300 mg CBA intravenously over 30 minutes every 12 hours for CrCl 50 ml/min/1.73 m2. Thrice daily every 8 hours if CrCl 30 ml/min/1.73 m2. PO twice daily every 12 hours. 2. CBT calculated using MTTW equation

**Garonzik et al.**

- n=28
- Septic patients (bloodstream infections 64.3%) and ventilator-associated pneumonia (35.7%)
- Colistin MICs 0.19 – 1.5 mg/L
- Dosing (infused over 30 minutes)
  - Loading dose (LD) CMS 300 mg CBA
  - CrCl >50 150 mg CBA every 12 hours
  - CrCl 20-50 150 mg CBA every 24 hours
  - CrCl <20 150 mg CBA every 48 hours

**Dalfino et al.**

- Clinical cure 82.1% (23/28)
- Bacteriological clearance 73.9% (17/24)
- No deterioration of renal function 82.1% (23/28)
- Acute kidney injury in 17.8% after ~7 days of therapy
- No renal replacement therapy needed in any patients

**Comparison Dosing Regimens**

<table>
<thead>
<tr>
<th>Manufacturer US</th>
<th>Garonzik et al.</th>
<th>Dalfino et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No loading dose for intermittent infusion</td>
<td>Loading dose recommended</td>
<td>Loading dose recommended</td>
</tr>
<tr>
<td>N/A</td>
<td>Loading dose based on weight / CrCl (max 300 mg CBA)</td>
<td>Fixed loading dose (300 mg CBA)</td>
</tr>
<tr>
<td>No HD/CRRT</td>
<td>HD/CRRT recommendations</td>
<td>No HD/CRRT recommendations</td>
</tr>
<tr>
<td>Intermittent dose</td>
<td>Calculated intermittent dose</td>
<td>Fixed intermittent dose</td>
</tr>
<tr>
<td>Frequency modified based on renal function - ranges</td>
<td>Frequency modified based on renal function - ranges</td>
<td>Frequency modified based on renal function</td>
</tr>
</tbody>
</table>

**Combination Therapy**

- Synergistic bactericidal activity
- Prevent bacterial regrowth
  - Seen shortly after initial exposure to colistin
- Optimal dosing strategies unestablished
  - Lower dose versus high dose
  - Intermittent versus continuous infusion
- Choice of combination agent
  - Multiple agents studied

**Activity Instructions**

- Think of one positive and one negative aspect of the dosing strategies in the two trials presented above.
- Think of one reason why combination therapy is advantageous for patients receiving colistin.
- Share and discuss with partner.

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THANK YOU
Pharmacy Practice Pearls

**Colistin Dosing: A Literature Review**

Kanan Shah, PharmD

0121-0000-14-018-L04-P

Learning Assessment Questions

1. In the study by Garonzik et al., what is the risk of using the recommended dosing strategy?
   a. Dosing strategy has not been validated to achieve clinical cure
   b. Dosing strategy has been validated to achieve microbiological eradication
   c. Dosing strategy will achieve Css-avg above 10 mg/L
   d. Dosing strategy is based on >800 colistin blood samples

2. Combination therapy with colistin may be advantageous over colistin monotherapy because
   a. colistin monotherapy serum level above MIC are reliably achieved in most patients
   b. combination therapy with colistin may prevent bacterial regrowth
   c. dosing strategies for colistin are well established in combination therapy regimens
   d. dosing strategies for colistin are well established in monotherapy regimens