Pharmacy Practice Pearls

Clinical Impact of a Pharmacist in Discharge Medication Reconciliation

Teresa Chu, PharmD
Swedish Covenant Hospital
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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 (ie: home → inpatient → discharge). (61% incomplete med hx on admission, 33% discharged pts with med-related problems)[1]
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? Are continued home medications appropriate? Are prophylactic drugs included?	Match the drug with patient's problem list. Prescribing should be evidence-based.
Are all medications at optimal/ target doses? 52.2% of discharge medication profiles require dose adjustments[2]	Medications should be dosed according to the most current treatment guidelines.

Clinical Interventions (cont.)

Recommend to discontinue medications without appropriate indications.	Eliminate duplications and reduce risk for drug-induced adverse events.
Recommend to add omitted medications if indicated.	For disease-state management and prevention of co-morbidities.
20% of discharge medication profiles requires the discontinuation or addition of medication(s)[2]	

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]

* Hypothesis generated for future randomized studies to confirm results

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

Swedish Covenant Hospital[4]

- 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

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

Swedish Covenant Hospital (cont.)

- Subjects divided into 2 groups:
  - Control: non-pharmacist involved discharge process
  - Intervention: med reconciliation and counseling by pharmacist at discharge
- All patients were contacted via phone for follow-up interviews
  - 1-2 weeks post-discharge: med compliance assessment (MMAS questionaire[6])
  - 30-45 days post-discharge: hospital readmission assessment and med compliance assessment (MMAS questionaire[6])
- Results and data evaluation in progress

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Pharmacy Practice Pearls

Clinical Impact of a Pharmacist in Discharge Medication Reconciliation

Teresa Chu, PharmD

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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

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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 care[1]
  - Avoidable cost opportunity from medication errors is $20 billion (range $15-28 billion)[1]
- 450,000 adverse drug events occur annually[2]
  - 25% of these medication errors are preventable[2]
- Technology has been introduced to improve accuracy of the medication use system[2]

National Data for Use of Technology in Hospitals

- 30% use computerized provider order entry[3]
- 50% use barcoded medication administration[3]
- 65% of clean rooms were compliant with Chapter 797 guidelines for CSPs[4]
- 11% use robots[4]
- 18% use carousels[4]

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

SCH Inpatient Pharmacy Pre-Remodel

Oral Solid Medication Storage

Pharmacist Work Stations

Remodeled SCH Inpatient Pharmacy

Overview with Centralized Med Storage & Dispensing Robot

Pharmacist Work Stations

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[5,6]

- 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[5,6]

- Designated, separate, well-light area
- 68ºF 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

Chapter 797 Environmental Control Requirements[5,6]

Clean Room	ISO Class
Ante Area	ISO Class 8
Buffer Area	ISO Class 7
Direct Compounding Area	ISO Class 5
Laminar Airflow Workbench (LAFW) or Compounding Aseptic Containment Isolator (CACI)	ISO Class 5

Chapter 797 Recommended Action Levels for Microbial Contamination[5,6]

ISO Class	Surface Sample (Contact Plate) (cfu per plate)
8	> 100
7	**> 5**
5	**> 3**

Surface sampling to be conducted every 6 months

Clean Room Pre-Remodel

Ceiling with Dust Pockets

Cooling and Air Filtration System

Remodeled Clean Room

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

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

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Questions?

ICHP 2014 Spring Meeting: Taking Bold Steps for Patient Care

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 work bench?
   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

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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 problem

- The resulting risk is neglect of liver disease
  - When selecting medications
  - When dosing medications
- Those with severe liver disease are vulnerable
  - Liver is key site of drug metabolism
  - Severe liver disease increases side effect risk

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

	1 point	2 points	3 points
Total bilirubin (mg/dl)	< 2	2 – 3	> 3
INR	< 1.7	1.7 – 2.3	> 2.3
Albumin (g/dl)	> 3.5	2.8 – 3.5	< 2.8
Ascites	none	controlled	refractory
Hepatic encephalopathy	none	mild	poorly controlled

Applicable to those with cirrhosis
Score ranges from 5 to 15

The Child-Pugh score

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

Patient case #1

Attribute	Child-Pugh points
No ascites	1
No hepatic encephalopathy	1
INR = 2.0	2
Tbil = 1.1 mg/dl	1
Albumin = 2.0 g/dl	3
Large esophageal varices	NA

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?

Patient case #2

Attribute	Child Pugh points
No ascites	1
No hepatic encephalopathy	1
INR = 1.3	1
Tbil = 0.9 mg/dl	1
Albumin = 3.8 g/dl	1
No varices	NA

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
  - dipyramidole

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

1. Centers for Disease Control and Prevention. National Vital Statistics Reports: Deaths: Final Data for 2010. Available at http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_04.pdf. Accessed February 15, 2014.

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Reading list

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Drug Choice and Dosing in the Patient with Advanced Liver Disease
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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:
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Conflict of Interest Declaration

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

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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.

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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

MacLaren G, Spelman D. Colistin: an overview. In: *UpToDate, Hooper DC (Ed), UpToDate, Waltham, MA, 2005.*

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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

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 (6):2274-2275.

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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

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Manufacturer Recommended Dosing

USA Colistimethate (expressed in mg CBA)

	Normal Renal Function	Mild Renal Impairment	Moderate Renal Impairment	Considerable Renal Impairment
Plasma Creatinine (mg/100mL)	0.7 – 1.2	1.3 – 1.5	1.6 - 2.5	2.6 - 4
Urea Clearance (% normal)	80 - 100	40 - 70	25 - 40	10 - 25
Unit Dose CMS (mg)	100 - 150	75 - 115	66 - 150	100 - 150
Frequency (times/day)	4 - 2	2	2 - 1	Every 36 hours
Total Daily Dose (mg)	300	150 - 230	133 - 150	100
Approximate Daily Dose (mg/kg/day)	5	2.5 - 3.8	2.5	1.5

Colistimethate for injection [package insert]. Big Flats, NY: X-gen Pharmaceuticals Inc; 2010.

Manufacturer Recommended Dosing USA Colistimethate

- 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

Colistimethate for injection [package insert]. Big Flats, NY: X-gen Pharmaceuticals Inc; 2010.

Do you have a protocol at your institution that adheres to this regimen?

A. Yes – exactly
B. Yes – modified
C. No

Resistance Breakpoints

	CLSI*	EUCLAST§
Acinetobacter spp.	≥4 mg/L	>2 mg/L
Pseudomonas aeruginosa	≥8 mg/L	>4 mg/L

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

European Committee on Antimicrobial Susceptibility Testing. Colistin: Rationale for the clinical breakpoints, version 1.0, 2010. http://www.eucast.org.
Biswas S, Brunel J, Dubus J, Reynaud-Gaubert M, Rolain J. Colistin: an update on the antibiotic of the 21st century. *Expert Rev Anti Infect Ther.* 2012;10(8):917-934.

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

Plachouras D, Karvanen M, Friberg LE, et al. Population pharmacokinetic analysis of colistin methanesulfonate and colistin after intravenous administration in critically ill patients with infections caused by gram-negative bacteria. *Antimicrob Agents Chemother.* 2009;53(8):3430-3436.

Plachouras et al.

Dosing Strategy	Time to Reach Peak >2mg/L
100 mg (15 min infusion) Q8H	>36 hrs
300 mg (15 min or 2 hr infusion) X1 dose then 150 mg (15 min infusion) Q12H	>12 hrs
400 mg (15 min or 2 hr infusion) X1 dose then 15 0mg (15 min infusion) Q12H	<12 hrs

Plachouras D, Karvanen M, Friberg LE, et al. Population pharmacokinetic analysis of colistin methanesulfonate and colistin after intravenous administration in critically ill patients with infections caused by gram-negative bacteria. *Antimicrob Agents Chemother.* 2009;53(8):3430-3436.

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

Garonzik SM, Li J, Thamlikitkul V, et al. Population pharmacokinetics of colistin methanesulfonate and formed colistin in critically ill patients from a multicenter study provide dosing suggestions for various categories of patients. *Antimicrob Agents Chemother*. 2011;55(7):3284-3294.

Garonzik et al.

	Median	Range
CrCl (ml/min/1.73m^2)	28.7	0 - 169
Daily CBA dose (mg)	200	75 - 410
$C_{ss,avg}$ [1] (mg/liter)	2.36	0.48 - 9.38

1. Average steady-state plasma concentration

Garonzik SM, Li J, Thamlikitkul V, et al. Population pharmacokinetics of colistin methanesulfonate and formed colistin in critically ill patients from a multicenter study provide dosing suggestions for various categories of patients. *Antimicrob Agents Chemother*. 2011;55(7):3284-3294.

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Garonzik et al.

Dose	Patient Population	Dose calculation[2]
Loading	All patients	CBA (mg) = colistin $C_{ss\text{-}avg}$ target X 2 X body wt (kg) Max: 300mg CBA
Maintenance Dose (24hr after loading dose)	No renal replacement	Daily dose CBA (mg)[1] = colistin $C_{ss\text{-}avg}$ target X (1.5 X CrCL[2] +30) Max: 300mg CBA
	Intermittent HD	Daily dose CBA (mg)[3] = colistin $C_{ss\text{-}avg}$ target X 30 Supplemental dose: Add 50% daily dose if admin last hour of HD OR 30% daily dose if admin after HD
	CRRT	Daily dose CBA (mg)[4] = colistin $C_{ss\text{-}avg}$ target X 192

1. Interval for CrCl<10ml/min/1.73m2 dose every 12 hours; for CrCl 10-70ml/min/1.73m2 dose every 8-12 hours; CrCl >70ml/min/1.73m2 dose every 8-12 hours
2. CrCl calculated using Jelliffe equation
3. Twice daily dosing recommended
4. Dosing every 8 – 12 hours recommended

Garonzik SM, Li J, Thamlikitkul V, et al. Population pharmacokinetics of colistin methanesulfonate and formed colistin in critically ill patients from a multicenter study provide dosing suggestions for various categories of patients. *Antimicrob Agents Chemother*. 2011;55(7):3284-3294.

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Dalfino 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 L, Puntillo F, Mosca A, et al. High-dose, extended-interval colistin administration in critically ill patients: is this the right dosing strategy? A preliminary study. *Clin Infect Dis.* 2012;54(12):1720-1726.

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Dalfino et al.

- Clinical cure 82.1% (23/28)
- Bacteriological clearance 73.9% (17/28)
- 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

Dalfino L, Puntillo F, Mosca A, et al. High-dose, extended-interval colistin administration in critically ill patients: is this the right dosing strategy? A preliminary study. *Clin Infect Dis.* 2012;54(12):1720-1726.

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Comparison Dosing Regimens

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

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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

Poudyal A, Howden BP, Bell JM, et al. In vitro pharmacodynamics of colistin against multidrug-resistant Klebsiella pneumoniae. *J Antimicrob Chemother.* 2008;62(6):1311-1318.

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.

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