Continuous Renal Replacement Therapy Based Dose Adjustments - Adult - Inpatient Clinical Practice Guideline

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CPG Contact for Content:
Name:Jeff Fish, PharmD, BCCCP - Pharmacy
Phone Number: (608) 263-1290
Email Address:jfish@uwhealth.org

Name:Cindy Gaston PharmD, BCPS- Pharmacy
Phone Number: (608) 265-8161
Email Address:cgaston@uwhealth.org

CPG Contact for Changes:
Name: Philip J Trapskin, PharmD, BCPS – Drug Policy Program Manager
Phone Number: (608) 263-1328
Email Address: ptrapskin@uwhealth.org

Guideline Author(s):
Jeff Fish, PharmD, BCCCP
Ryan Draheim, PharmD
Chris Viesselmann, PharmD

Coordinating Team Members:
J. Fish, PharmD, BCCCP

Review Individuals/Bodies:
A.Yevzlin, MD; L. Schulz, PharmD, BCPS; Cindy Gaston, PharmD, BCPS

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Executive Summary

Guideline Overview

These clinical practice guidelines are intended to guide pharmacists in the dosing of medications in adult intensive care unit (ICU) patients receiving continuous renal replacement therapy (CRRT).

Key Practice Recommendations

1. The CRRT dose adjustment table should be used in adult ICU's at UW Health to guide medication dosing for patients receiving CRRT (CVVH or CVVHD) to maximize drug therapy, ensure appropriate drug dosing, and standardize CRRT based dose adjustments (Appendix A). **(Class I, Level C)**
2. Medication dose adjustments should be performed by the clinical pharmacist according to the "Continuous Renal Replacement Therapy (CRRT)-Based Dose Adjustments Delegation Protocol – Adult – Inpatient" **(Class I, Level C)**

Companion Documents

1. UW Health Renal Function-Based Dose Adjustment -Adult – Inpatient/Ambulatory Clinical Practice Guideline

Pertinent UW Health Policies & Procedures

1. Continuous Renal Replacement Therapy (CRRT)-Based Dose Adjustments Delegation – Adult – Inpatient Protocol
2. Renal Function-Based Dose Adjustments - Adult – Inpatient/Ambulatory Protocol

Scope

Clinical Specialty:

This guideline may be used by any prescriber or pharmacist treating an adult patient undergoing CRRT in an ICU to identify appropriate dosing of medications based on ultrafiltration rate and patient weight.

Intended Users:

Physicians, pharmacists, mid-level providers, and nurses

Objective(s):

The objective of this guideline is to facilitate the appropriate dosing of medications in adult ICU patients receiving CRRT based on patient and therapy-specific pharmacokinetic calculations.

Target Population:

Critically ill adult patients receiving CRRT therapy in an ICU

Interventions and Practices Considered:

This guideline provides patient and therapy-specific dosing recommendations based on each medication's unique pharmacokinetic parameters, ultrafiltration rate and patient weight.

Major Outcomes Considered:

The major outcome considered in this guideline is the appropriate dosing of medications in patients receiving CRRT. Efficacy is measured by the rate of clinical cure of infection for antimicrobials and drug efficacy for other medications. Safety is measured as the rate of clinical failure and the occurrence of adverse events due to medications.

Guideline Metrics:

Literature will be periodically reviewed to determine new recommendations for dosing medications in CRRT. Patient Safety Net events (PSNs) related to medication therapy in patients receiving CRRT are reviewed throughout the year.

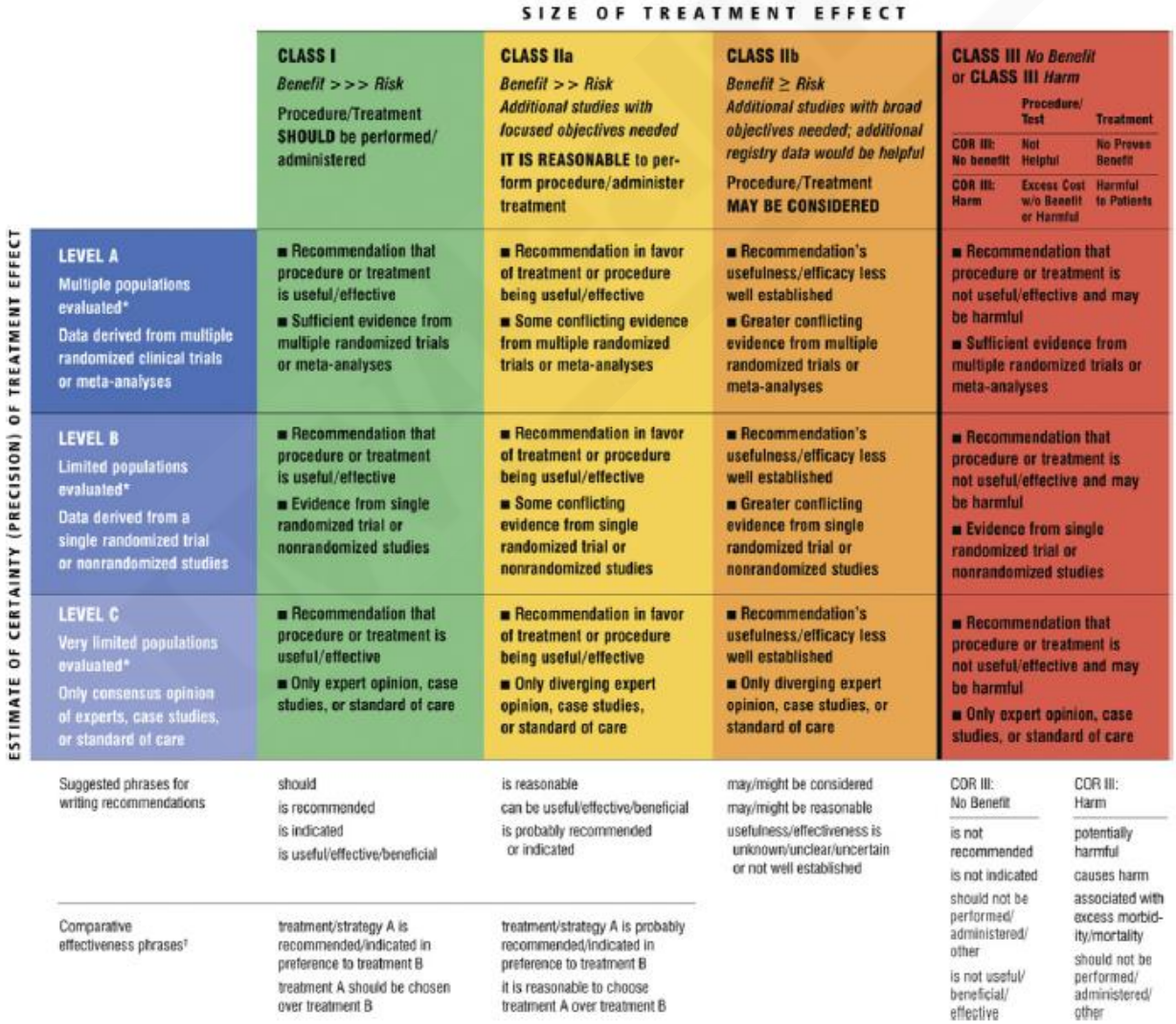
Methodology

Methods Used to Collect/Select the Evidence:

Completed a comprehensive literature search of electronic databases (Micromedex, LexiComp, eFacts); conducted an in-depth review of relevant abstracts and articles; conducted a thoughtful discussion and interpretation of findings; ranked strength of evidence underlying the current recommendations that have been provided.

Rating Scheme for the Strength of the Evidence and Recommendations:

A modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology was used to assess the Quality and Strength of Evidence in this Clinical Practice Guideline.[1]



ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT: CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

Methods Used to Formulate the Recommendations:
Recommendations were based on strength of evidence and clinical expert consensus.

Definitions
1. Slow continuous ultrafiltration (SCUF): a type of CRRT used to remove excess fluid in fluid overloaded patients. Fluid is removed via ultrafiltration and no replacement or dialysis fluids are utilized.
2. Continuous venovenous hemofiltration (CVVH): a type of CRRT that utilizes convection for fluid and solute removal. Replacement fluids are utilized in CVVH.
3. Continuous venovenous hemodialysis (CVVHD): a type of CRRT that utilizes diffusion for fluid and solute removal. Dialysis fluids are utilized in CVVHD.
4. Equations and formulas[2]
   - 4.1. $TBC = CL_{NR} + CL_{CRRT}$
     - 4.1.1. TBC = total body clearance
     - 4.1.2. CL_{NR} = clearance (non-renal)
     - 4.1.3. CL_{CRRT} = clearance via CRRT = renal clearance for anuric patients on CRRT
   - 4.2. $CL_{CRRT} = S \times UFR$
     - 4.2.1. S = sieving coefficient = concentration of drug in ultrafiltrate divided by the concentration of drug in the blood (may be estimated by fraction of drug unbound)
     - 4.2.2. UFR = ultrafiltrate flowrate of CRRT machine
   - 4.3. $CL_{NR} = Vd \times K_{HD}$
     - 4.3.1. Vd = volume of distribution (in dialysis patients if available)
     - 4.3.2. K_{HD} = elimination rate constant in dialysis patients
   - 4.4. $fr_{CRRT} = \frac{CL_{CRRT}}{TBC}$
     - 4.4.1. fr_{CRRT} = fraction of drug removed by CRRT
   - 4.5. $MDMF = \frac{1}{1 - fr_{CRRT}}$
     - 4.5.1. MDMF = maintenance dose multiplication factor
   - 4.6. $CRRT\ dose = MDMF \times anuric\ dose$

Introduction
Continuous renal replacement therapy (CRRT) is a dialysis mode common in ICUs, for its use in patients with severe hemodynamic instability.[3] Periods of volume overload and depletion, which are likely with intermittent hemodialysis, are minimized with CRRT due to the continuous regulation of fluid and nutrition, both enteral and parenteral. Appropriate dosing of medications in patients receiving CRRT is difficult to determine due to limited number of studies, small heterogeneous study populations and differing modes of CRRT and ultrafiltration rates in the studies. However, reliable dose adjustments can be made with the use of pharmacokinetic principles.[4]

A CRRT dose adjustment table was developed in Microsoft Excel at UW Health to assist providers with dose adjustments in patients receiving CRRT. The patient's weight and ultrafiltration rates are entered into the Excel spreadsheet to make the dose

adjustments patient specific. Adjustments may be made to the dose or dosing interval based on whether the drug has time dependent or concentration dependent pharmacodynamics. Pharmacokinetic parameters and recommended dosing regimens for CRRT were obtained from medication databases, clinical dosing markers, and/or published primary literature.[5-10]

Recommendations

3. The CRRT dose adjustment table should be used in adult ICU's at UW Health to guide medication dosing for patients receiving CRRT (CVVH or CVVHD) to maximize drug therapy, ensure appropriate drug dosing, and standardize CRRT based dose adjustments (Appendix A). **(Class I, Level C)**
4. Medication dose adjustments should be performed by the clinical pharmacist according to the "Continuous Renal Replacement Therapy (CRRT)-Based Dose Adjustments Delegation Protocol – Adult – Inpatient" **(Class I, Level C)** 4.1.**)**

UW Health Implementation

Potential Benefits:

1. Appropriately dosing antibiotics in ICU patients will improve patient outcomes.
2. Standardizing dosing of medications in ICU patients will provide consistency in patient treatment.

Potential Harms:

None anticipated

Implementation Plan/Tools

1. Guideline will be housed on U-Connect in a dedicated folder for CPGs.
2. Release of the guideline will be advertised in the Clinical Knowledge Management Corner within the Best Practice newsletter.
3. Links to this guideline will be updated in Health Link.
4. Critical care pharmacists will be trained on correct use of the CRRT dose adjustment table.
5. The guideline will be operationalized by pharmacists through a delegation protocol.

Disclaimer

CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

References

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Appendix A

Table 1. CRRT Dosing Table

UW Health CRRT table .xls