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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.⁷
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
   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. 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.

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.\textsuperscript{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). (\textbf{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” (\textbf{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


Appendix A

Table 1. CRRT Dosing Table