Comparison of Drug Dosing Equations for Continuous Renal Replacement Therapy (CRRT)

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Background

- Continuous renal replacement therapy (CRRT) is a commonly used method for solute and fluid management in critically ill patients.
- Although many CRRT drug dosing guidelines have been published, none have been prospectively validated.
- Three different drug dosing equations have been published.
  - **Equation A - Kroh** [1]
    Adjusted Dose = $D_n \times [P_x + (Q_F \times S_C/CL_n)]$
  - **Equation B - Bugge** [2]
    Adjusted Dose = $D_n \times [P_x + (1 - P_x) \times CL_{CRtot}/CL_{CRn}]$
  - **Equation C - Reetze-Bonorden** [3]
    Adjusted Dose = $D_{anuric} \times [1 - ((Q_F \times S_c)/(Q_F \times S_c + CL_{ANUR}))]$

D_n: Normal dose in healthy adults
D_{anuric} : Maintenance dose for anuria
$P_x = CL_{ANUR}/CL_N$: Extra-renal clearance fraction
CL_{ANUR}: Non-renal drug clearance in anuria
CL_N: Normal drug clearance
$Q_F = CL_{CRtot}$: CRRT effluent flow rate
S_C: Sieving coefficient
CL_{CRn}: Creatinine clearance in healthy adults

Purpose

- To compare the four literature-based CRRT dosing recommendations for 10 commonly used antibiotics.

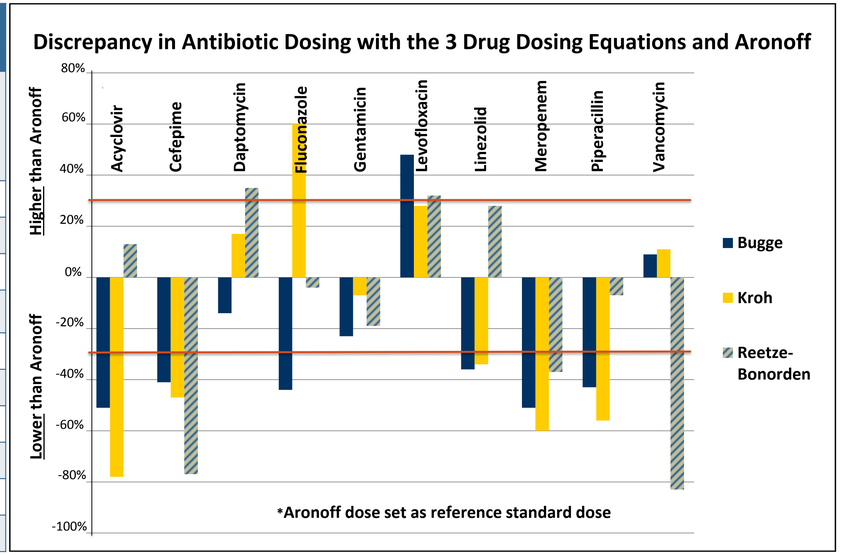
Methods

- A prospective literature search was conducted to obtain pharmacokinetic parameters for 10 commonly used antibiotics:
  - Acyclovir, cefepime, daptomycin, fluconazole, gentamicin, levofloxacin, linezolid, meropenem, piperacillin, and vancomycin
- A hypothetical 70 kg patient with Acute Kidney Injury on CRRT with an effluent rate of 25ml/min (23.3 ml/kg/hr) based on the KDIGO CRRT effluent rate recommendations was modeled.
- The antibiotic doses were calculated using three different CRRT drug dosing equations (Kroh, Bugge, and Reetze-Bonorden) and standardized to mg/day to facilitate comparison.
- Doses were compared to Aronoff et al book [4] which was used as the reference comparator.
- Clinically significant discrepancy between the calculated dose and the Aronoff dose was set at ≥ 30 %.
- Descriptive statistics were used to compare the calculated doses.

Results

Recommended Antibiotic Doses by Different Dosing Resources

Drug Name	Aronoff (mg/d)	Bugge (mg/d)	Kroh (mg/d)	Reetze-Bonorden (mg/d)
Acyclovir	525	260	117	592
Cefepime	4,000	2,363	2,150	935
Daptomycin	280	242	328	378
Fluconazole	400	225	640	386
Gentamicin	120	94	113	98
Levofloxacin	250	370	319	328
Linezolid	1,200	770	797	1,526
Meropenem	3,000	1,477	1,227	1,899
Piperacillin	12,000	6,882	5,370	11,181
Vancomycin	1,000	1,083	1,109	179



Conclusions

- This study unveils a wide variability among antibiotic dosing recommendations from published CRRT dosing equations that can potentially lead to inappropriate pharmacotherapy.
- Limitations of the study include:
  - This study was not designed to show which method is best.
  - Dosing recommendation from Aronoff is based on an effluent rate of 33 ml/min.
- Prospective evaluation of antibiotic dosing schemes with pharmacokinetic trials are needed.

References

1. Kroh UF. New Horiz 1995;3(4):748-759
2. Bugge JF. Acta Anaesthesiol Scand 2001;45(8):929-934
3. Reetze-Bonorden P, et al. Clin Pharmacokinet 1995;24(5):362-379
4. Aronoff GR, et al. American College of Physicians 2007;17-131

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Abstract

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Methods

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