

DIALYZE-IHD: Dialyzability of Medications in Patients Undergoing Intermittent Hemodialysis

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Background

- Patients in the HD units are utilizing high-flux, high-efficiency, intermittent hemodialysis (IHD)
- Appropriate medication use in the IHD population requires dose scheduling around dialysis sessions, and at times, the use of dose supplementation
- The pharmacokinetic properties of a medication and its dialyzability aides in deciding the dosing regimen, including:
 - Molecular Weight (MW)
 - Excreted Unchanged (EU)
 - Half-life ($t_{1/2}$)
 - Plasma Protein Binding (PPB)
 - Volume of Distribution (Vd)
 - Type of Dialysis Membrane - measure of ultrafiltration capacity (K_{uf} - ultrafiltration coefficient)
 - High Flux – $K_{uf} > 20\text{mL/hour/mm Hg}$, e.g. polysulfone
 - Low Flux – $K_{uf} < 10\text{mL/hour/mm Hg}$, e.g. cellulose acetate

Objectives

- To determine the dialyzability of commonly used medications in hemodialysis patients
- To provide dosing recommendations for IHD patients, based on reviewed literature on dialyzability, pharmacokinetic properties and clinical practice

Methods

- Comprehensive literature search was conducted
- Primary literature reviewed: dated from 1970s to present
- MeSH Terms: hemodialysis, intermittent hemodialysis, pharmacokinetics, dialyzability, drugs & drug class
- Secondary References: PubMed/Medline, EMBASE, International Pharmaceutical Abstract
- Tertiary References: Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children (Aronoff et al.) 5th Ed. , Dialysis of Drugs 2011 (Ballie et al.)
- Search Exclusion: peritoneal dialysis, continuous renal replacement therapy, hemodiafiltration, plasmapheresis, detoxification dialysis

Results

Drug	MW* (Da)	EU(%)**	Normal $t_{1/2}$ (Hours)**	ESRD $t_{1/2}$ (Hours)**	PPB (%)**	Vd (L/kg)**	Dialytic Plasma Clearance (mL/min)	% Dialyzed	IHD Dosing	IHD Dosing Adjustment
ACE Inhibitors										
Captopril	217	40-50	2-3	21-32	25-30	0.7-3	N/A	40 (high flux)	12.5mg Q24H	Dose Post-HD
Enalapril	376	88	11-24	34-60	50-60	1-2.4	38.8-42	37.8-57 (low flux)	2.5mg Q24H	Dose Post-HD
Lisinopril	405	88-100	30	40-50	0	1-3.8	34.4-47.7	50.5 (low flux)	2.5mg Q24H	Dose Post-HD
Quinapril	438	30	1-2	6-15	97	1.5	15.4	11.7 (low flux)	2.5mg Q24H	No Adjustment
Ramipril	416	35	8-10	14-16	55-70	1.2	23.3	Minimal (low flux)	2.5mg Q24H	Dose Post-HD
Trandolapril	430	33	6-10	N/A	65-94	0.26	N/A	Minimal (N/A)	0.5mg Q24H OR 2mg QHD (thrice weekly)	No Adjustment
Penicillins										
Amoxicillin	365	50-70	0.9-2.3	5-20	15-25	0.26	58.9-83.6	30-64 (low flux)	500mg Q24H	Dose Post-HD
Ampicillin	349	30-90	0.8-1.5	7-20	20	0.17-0.31	30-61	35-40 (low flux)	1g IV Q12H	Dose Post-HD
Cloxacillin	436	35-70	0.7	1-2	95	0.16	N/A	N/A	250-500mg PO QID or 1-2g IV Q4-6H	No Adjustment
Penicillin G	334	60-85	0.5	6-20	50	0.3-0.42	N/A	N/A	1-4 million units Q12-18H	Dose Post-HD
Penicillin V	350	26-65	0.6	4.1	75-89	0.5	N/A	N/A	300mg Q12H	Dose Post-HD
Piperacillin/Tazobactam***	518/300	75-90/65	0.8-1.5/1	3.3-5.1/17	30/22	0.18-0.30/0.21	29.0-78.2/94.6	10-65/37-39 (low flux)	2.25-4.5g Q12H	Dose Post-HD
Macrolides										
Azithromycin	749	6-12	10-60	N/A	8-50	18	8.3	N/A	500mg Q24H	No Adjustment
Clarithromycin	748	20-30	2.3-6.0***	22***	70	2-4	N/A	N/A	250-500mg Q24H	Dose Post-HD
Erythromycin	734	15	1.4	5-6	60-95	0.6-1.2	28.5	0.02-6.96 (low flux)	250-500mg PO QID or 250mg IV Q6H	No Adjustment

*MW available from DrugBank, **Pharmacokinetic data available from Aronoff et al., *** Pharmacokinetic data available from Heintz et al. Antimicrobial Dosing Concepts and Recommendations for Critically Ill Adult Patients Receiving Continuous Renal Replacement Therapy or Intermittent Hemodialysis. Pharmacotherapy 2009;29(5):562-77.
N/A = Data Not Available from sources noted above and from primary literature

Table 1: Dialyzability and Dosage Recommendations of Commonly Prescribed Medications (Sample)

Limitations

- The primary literature reviewed mainly consisted of pharmacokinetic studies, observational studies, case studies or case reviews
- Due to the limited primary literature available, both low flux and high flux dialysis data were included (as shown by parenthesis in the table above)
- Dosing recommendations provided are based on a combination of pharmacokinetic interpretation, dialyzability literature and clinical practice

Results

- Drug Classes Reviewed: (n = 141)
- ACE Inhibitors
 - Alpha Blockers
 - Aminoglycosides
 - Analgesics
 - Anemia Medications
 - Angiotensin II Receptor Blockers
 - Antibiotics (Misc.)
 - Antifungals
 - Anti-Rejection Medications
 - Antivirals
 - Beta Blockers
 - Calcium Channel Blockers
 - Carbapenems
 - Cardiovascular Medications (Misc.)
 - Cephalosporins
 - Diabetes Medications
 - Dyslipidemia Medications
 - Intradialytic Medications
 - Macrolides
 - Metabolic Bone Disease Medications
 - NSAIDs
 - Opioids
 - Penicillins
 - Psychotropics
 - Quinolones
 - Sedatives
 - Statins
 - Tetracyclines

Conclusions

- Dialyzability data gathered in DIALYZE-IHD is current as of April 2012
- DIALYZE-IHD website & mobile site will be available for access starting September 2012
- Nursing intermittent hemodialysis dosing guide poster will be available in the dialysis clinic at St. Paul's Hospital and at Community Dialysis Units



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