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NOVEL PRACTICE SITE

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In July 2010, the Illinois Department of Corrections (IDOC) and University of Illinois at Chicago entered into a contract to provide specialized telemedicine services in HIV to prisoners within the State of Illinois. Telemedicine incorporates a multidisciplinary approach to improve patient safety and efficacy of medication therapy, construction of antiretroviral therapy, and assessing for and managing side effects and drug interactions. The overall goal of the telemedicine practice site is to enhance the quality of specialty care provided to those that are HIV positive and incarcerated in the IDOC system.

Since 2011, the program provides care to twenty-eight adult correctional facilities through a multidisciplinary approach between physicians, clinical pharmacists, case management, information technology, and scheduling. Although slightly different from a face-to-face encounter, a telemedicine appointment is very similar to that of a traditional exam with the exception that the patient has access to physicians, pharmacists, and case managers simultaneously.

The clinical pharmacists practice in a very unique setting where they are responsible for educating those incarcerated on their specialty medications, with respect to administration, dosing, and potential side effects/drug interactions, and the importance of medication adherence. In addition, clinical pharmacists work to identify and construct antiretroviral regimens for antiretroviral naïve and treatment-experienced patients. This specialty clinic site is offered as a rotation to pharmacy students and post-graduate residents and fellows.

For even more Adult Med PRN News and member accomplishments, be sure to read the upcoming ACCP PRN News Report!

In this issue:

PRN OFFICERS

HUNTSVILLE HOSPITAL ANTIMICROBIAL MANAGEMENT TEAM (AMT)

AUTHOR: MICKALA M. THOMPSON, PHARM.D., BCPS

The Antimicrobial Management Team (AMT) of Huntsville Hospital is a multidisciplinary antimicrobial stewardship cohort developed in 2010 in response to increasing nosocomial infection rates and rising drug expense. The AMT initiative represents a collaborative effort of the Infection Control Committee, Microbiology Department, and the Anti-Infective Subcommittee of the Pharmacy and Therapeutics Committee, which are supported by the Medical Executive Committee (MEC). The AMT pharmacists include Edward H. Eiland, III, Pharm.D., MBA, BCPS, FASHP, **Jonathan D. Edwards**, Pharm.D., BCPS, and **Mickala M. Thompson**, Pharm.D., BCPS.

Daily Activities of the AMT

The designated AMT pharmacist devotes 3 hours daily to AMT activities. The pharmacist reviews patient medication profiles to identify clinical involvement opportunities and collaborates with an assigned ID physician to provide antimicrobial therapy recommendations.

The AMT identifies patients on antibiotics without a clinical indication, or patients requiring antimicrobials but on suboptimal or excessive therapy based on indication, dose, or therapy duration.

The AMT also:

• Enforces utilization of treatment algorithms (e.g. *C. difficile* Infection (CDI) Clinical Pathway).

• Ensures compliance with carbapenem and echinocandin formularies.

• Identifies candidates for IV anti-infective therapy at Huntsville Hospital Outpatient Medical (OPM).

AMT Successes

The AMT continues to facilitate a decreasing antibiotic cost per adjusted discharge, from $81.06 in FY10 to $73.05 in FY13, which correlates to a $2.18M aggregate cost avoidance. Additional impacts include decreased antimicrobial resistance, more discriminate use of new anti-infective agents, improved patient outcomes impacting length of hospitalization, improved healthcare provider education, and increased outpatient revenue (utilization of 340b antimicrobial pricing through OPM).

The AMT was presented the Bright Ideas Award in Quality Improvement at the 2012 VHASE Annual Trustee Conference and was a silver level recipient in the health care category at the 2012 Alabama Performance Excellence Award Conference.

MEMBER ACCOMPLISHMENTS

- **Melissa Badowski**, PharmD received an HIV Practice Award from the American Academy of HIV Medicine and Institute for Technology for the use of technology at her practice site
- **Jonathan Edwards**, BCPS and **Diane Goodwin**, PharmD, BCPS, FCCP achieved Board Certification in Pharmacotherapy
- **Beth H. Resman-Targoff**, PharmD, FCCP presented “Their Own Worst Enemy: Helping Patients with Autoimmune Diseases” at the 2013 American Pharmacists Association Annual Meeting in Los Angeles, CA
- **Leslie Richard**, Pharm.D., CGP achieved Board Certification in Geriatrics
- **Sharon See,** Pharm.D., BCPS, FCCP was named to the Pharmacotherapy Specialty Council of the Board of Pharmaceutical Specialties
- **Sharon See,** Pharm.D., BCPS, FCCP was selected as a 2013 Vincentian Research Fellow for St. John's University

MEMBER PUBLICATIONS

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- **Woytowish MR,** Maynor LM, Clinical Relevance of Linezolid-Associated Serotonin Toxicity. Ann Pharmacother 2013; 47: 388-397.

Congratulations

Amed PRN 2012 Fellows of the American College of Clinical Pharmacy (FCCP)

Shareen El-Ibiary, Pharm.D., BCPS, FCCP	Midwestern University, Glendale AZ
Brian A. Hemstreet, Pharm.D., BCPS, FCCP	University of Colorado, Denver, CO
Julie A. Murphy, Pharm.D., BCPS, FCCP	University of Toledo, OH

TREATMENT OPTIONS FOR MINERAL AND BONE DISORDERS ASSOCIATED WITH CHRONIC KIDNEY DISEASE

AUTHOR: STACY ELDER, PHARM.D., BCPS
ASSISTANT PROFESSOR, PHILADELPHIA COLLEGE OF PHARMACY

Chronic kidney disease (CKD) is estimated to affect 5-10% of the world population. CKD-mineral and bone disorders (MBD) begin to occur early in the disease process.[1,2] CKD-MBD is defined as a systemic disorder of mineral and bone metabolism, secondary to CKD, that includes abnormalities of calcium, phosphorus, parathyroid hormone (PTH) or vitamin D metabolism; abnormalities in bone turnover, mineralization, volume, linear growth or strength; or vascular or soft tissue calcification.[2]

As renal function declines, phosphorus is excreted less effectively and serum phosphorus level increases over time. This increase in phosphorus in patients with CKD is associated with an increased risk of mortality, cardiovascular events, and secondary hyperparathyroidism (SHP).[1,3-5] Patients with hyperphosphatemia secondary to CKD may have subsequent elevations in PTH and are at an increased likelihood of vitamin D deficiency due to decreased conversion to the active form (calcitriol) by the kidney. Deficiency in vitamin D results in an increased risk of morbidity and mortality, as well as impaired calcium absorption from the gastrointestinal (GI) tract.[6,7] Low levels of vitamin D and serum calcium, as well as phosphate retention, are all risk factors for overproduction of PTH, particularly as the kidney becomes less responsive to the hormone in patients with CKD.[8] SHP perpetuates further release of calcium and phosphorus from bone, ultimately leading to poor patient outcomes including fractures and hospitalizations.[1,4,9] For treatment of CKD-MBD, three pharmacologic targets can be utilized: phosphate binding agents can be used for treatment of hyperphosphatemia, vitamin D supplementation or receptor agonists for treatment of vitamin D insufficiency, and calcimimetics for treatment of SHP.

Standard hemodialysis and dietary restriction may be implemented to treat hyperphosphatemia but are typically not sufficient to maintain goal phosphate levels in patients with CKD. Phosphate binding agents are typically used in addition to these strategies and are often classified as either calcium-containing (carbonate or acetate) or noncalcium-containing (typically, sevelamer or lanthanum). All are effective at decreasing phosphate levels; however, dosing escalation of calcium-containing agents may be limited if hypercalcemia occurs. Comparatively, the noncalcium-containing agents are associated with more GI side effects and are typically more expensive than the calcium-containing agents. Studies have not conclusively elucidated one product as superior to others with regard to patient outcomes, but observational data suggest a survival advantage for CKD patients on phosphate binding agents as opposed to those who are not.[3] The 2003 KDOQI guidelines suggest a goal phosphate level of 1.12-1.77 mmol/L (3.46-5.48 mg/dL), while the 2009 KDIGO guidelines recommend a more conservative goal of 0.87-1.49 mmol/L (2.7-4.6 mg/dL) for non-dialysis CKD patients, based on data suggesting that mortality increases by 18% for every 0.32 mmol/L increase in serum phosphorus and other studies proving the harmful effects of hyperphosphatemia.[10]

Vitamin D deficiency, with or without hypocalcemia and SHP, can be treated with vitamin D replacement (cholecalciferol, ergocalciferol) or vitamin D receptor agonists (paricalcitol, doxercalciferol). Some studies, though biased, have shown that exogenous repletion of vitamin D significantly increases survival in CKD patients at various stages.[11,12] Additionally, a meta-analysis of studies in patients without CKD showed mortality and cardiovascular event reduction in patients who were not deficient in vitamin D.[13] Conversely, some studies did not show a benefit of vitamin D supplementation in patients with CKD.[14] Though this data seems contradictory, the general consensus is that the risk of supplementation with vitamin D is relatively low and a potential benefit exists.

TREATMENT OPTIONS FOR MINERAL AND BONE DISORDERS ASSOCIATED WITH CHRONIC KIDNEY DISEASE

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Aside from utilizing phosphate binders and vitamin D replacement or receptor agonists, SHP can also be treated with cinacalcet, a calcimimetic that increases the sensitivity of the calcium receptors to extracellular calcium. Increased sensitivity of calcium receptors results in decreased synthesis and secretion of PTH and, ultimately, lower serum calcium and phosphorus levels. In a study of dialysis patients, cinacalcet, in addition to a vitamin D receptor agonist, for the treatment of SHP showed a significant all-cause and cardiovascular mortality benefit.[15] However, a subsequent study that aimed to reduce the confounding by indication did not prove the same decrease in mortality or major cardiovascular events in a similar population of patients.[16] Although there is some controversy as to the true mortality benefit of calcimimetics, there are a number of trials proving it's utility in reducing PTH, parathyroidectomy, fractures, hospitalization and quality of life.[17]

Despite the compendium of data on CKD-MBD, an extraordinary number of questions remain unanswered regarding optimal treatment and prevention of poor outcomes in this patient population. As physiologic derangements commonly arise in patients with CKD, it is important to consider appropriate options for maintaining optimal bone health and take into consideration the true risks and benefits of therapy for this purpose.

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COMPARISON OF THE NEW ORAL ANTICOAGULANTS

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	Dabigatran (Pradaxa®)	Rivaroxaban (Xarelto®)	Apixaban (Eliquis®)
Mechanism of Action	Direct thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Indication(s) (U.S.)	Stroke prevention in nonvalvular atrial fibrillation	1) DVT/PE Treatment 2) DVT/PE Prophylaxis 3) Stroke prevention in nonvalvular atrial fibrillation 4) Post-op thrombophylaxis for hip or knee replacement	Stroke prevention in nonvalvular atrial fibrillation
Usual dose	150 mg PO BID	1) 15 mg PO BID for 3 weeks, then 20 mg PO daily 2) 20 mg PO daily 3) 20 mg PO daily 4) 10 mg PO daily	5 mg PO BID
Dose Adjustments	CrCl 15-30: 75 mg PO BID (Chest guidelines recommend avoiding if CrCl <30) CrCl <15: Avoid Discontinue in acute renal failure	CrCl 15-50 mL/min: 15 mg PO QDay CrCl <15 mL/min: avoid Discontinue in acute renal failure	2.5 mg PO BID if 2 of the following: • Age ≥ 80 • SCr ≥ 1.5 • Weight ≤ 60 kg
	P-gp inhibitors: CrCl 30-50:75 mg PO BID CrCl 15-30: avoid		Concomitant use of dual strong P-gp/CYP3A4 inhibitors: 2.5 mg BID
	Use in advanced liver disease is not recommended	Moderate to severe hepatic failure: avoid	Severe hepatic failure: avoid
	Consider avoiding in patients ≥ 80 years old		
Drug Interactions	Antithrombotics P-gp inducers P-gp inhibitors	Antithrombotics 3A4/P-gp inducers 3A4/P-gp inhibitors	Antithrombotics 3A4/P-gp inhibitors 3A4 inducers
Precautions/ Warnings	Bleeding: risk factors include concomitant use of antiplatelets and other antithrombotics, decreased renal function, and the elderly Valvular heart disease: Use is not recommended	Not recommended if lactose-intolerant BBW: use additional anticoagulant when discontinuing Discontinue at least 24 hours before surgery Valvular heart disease: Use is not recommended	Bleeding BBW: use additional anticoagulant when discontinuing Discontinue at least 48 hours prior to surgery Valvular heart disease: Use is not recommended
Pregnancy Category	C	C	B
Adverse Reactions	Dyspepsia Bleeding	Bleeding Headche, dizziness	Bleeding

COMPARISON OF THE NEW ORAL ANTICOAGULANTS

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	Dabigatran (Pradaxa®)	Rivaroxaban (Xarelto®)	Apixaban (Eliquis®)
Reversal	Dialyzable (60% over 2-3 hours) No specific reversal agent 4-factor PCC (Cofact) was **not** effective for reversal Other options may include FFP, packed RBCs, aPCC or rVIIa	Not dialyzable No specific reversal agent 4-factor PCC (Cofact) was effective for reversal	Not dialyzable No specific reversal agent
Pharmacokinetics			
Absorption	Rapid	Rapid	Rapid
Distribution	Vd=50-70L 35% protein bound	Vd=50L	Vd=21L 90% protein bound
Metabolism	Hepatic glucuronidation Substrate of P-gp	Hepatic (CYP3A4 and 2J2)	Hepatic (CYP3A4) Substrate of P-gp
Excretion	Urine	Urine	Urine
Monitoring	Routine anticoagulation monitoring not required Renal function aPTT, ECT, and TT can detect the presence of dabigatran CBC with differential	Routine anticoagulation monitoring not required Renal and hepatic function Anti-FXa preferred for detecting presence of rivaroxaban	Routine anticoagulation monitoring not required Renal and hepatic function Anti-FXa can detect presence of apixaban
Conversion from warfarin	Discontinue warfarin; Initiate dabigatran when INR < 2.0	Discontinue warfarin; Initiate rivaroxaban when INR < 3.0	Discontinue warfarin; Initiate apixaban when INR < 2.0
Conversion to warfarin	Initiation of warfarin dependent on renal function: CrCl>50: 3 days before discontinuing dabigatran CrCl 31-50: 2 days before discontinuing dabigatran CrCl 15-30: 1 day before discontinuing dabigatran CrCl<15: no recommendations	Initiate warfarin and a parenteral anticoagulant 24 hours after discontinuing rivaroxaban; discontinue the parenteral anticoagulant when INR is therapeutic	Initiate warfarin and parenteral anticoagulant when the next dose of apixaban is due; discontinue the parenteral anticoagulant when INR is therapeutic

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