MSHP Pharmascript

Volume 40, Issue No. 1
First Quarter

What's New with Flu 2015 to 2016

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If the weather outside is frightful, that means influenza season is once again underway. The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices has released their recommendations for the 2015-16 influenza season, with notable changes this year.

Influenza Prevention

It is important to encourage patients to receive an annual influenza vaccination. This year's flu vaccine formulation has been updated and contains different viral influenza strains compared to last year's vaccine. The trivalent vaccine has new influenza A (H3N2) and influenza B components. Trivalent vaccines contain hemagglutinin (HA) derived from an A/California/7/2009 (H1N1)-like virus, an A/Switzerland/9715293/2013 (H3N2)-like virus, and a B/Phuket/3073/2013-like virus. The quadrivalent vaccine contains an additional B/Brisbane/60/2008-like virus, which is identical to the quadrivalent formulations of the past few years.[1]

Along with new vaccine formulations there are new U.S. Food and Drug Administration (FDA)-approved vaccine products available this year. Afluria® (inactivated influenza vaccine, bioCSL, Inc., King of Prussia, Pennsylvania) uses the Stratis® needle-free jet injector (PharmaJet, Inc., Golden, Colorado), which is a spring-powered device that injects vaccine through a needle-free syringe into the deltoid muscle. This is the only inactivated flu vaccine that can be administered without a needle.

The FDA also expanded the age range for the egg-free influenza vaccine, Flublok® (Recombinant Influenza Vaccine, Trivalent [RIV3], Protein Sciences, Meriden, Connecticut), so that it is now indicated for people age 18 years and older (previously it was approved for those age 18 to 49).

The FDA approved the Fluzone® Intradermal Quadrivalent vaccine (Sanofi Pasteur, Inc., Swiftwater, Pennsylvania), for those aged 18 to 64 years. This product uses smaller needles to deliver vaccine to the skin, rather than muscle. It is expected that this formulation will replace the company's trivalent intradermal product.[1]

A nasal spray formulation of the influenza vaccine (FluMist®) contains the quadrivalent formulation of live attenuated virus. The nasal spray is approved for those aged 2 to 49 years old, and is especially useful in vaccinating children, as it is an alternative to

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injections. Of note, pregnant women, people with weakened immune systems and people who care for those with weakened immune systems should not receive the nasal formulation. Pregnant or post-partum women do not need to avoid contact with persons who recently received the nasal spray flu vaccine. [1]

While the CDC does not recommend a specific product for adults 65 and older, the Fluzone® High-Dose (HD) vaccine may be a superior option to the standard dose vaccine in this high-risk population. This vaccine contains four times the amount of influenza antigen (60 µg of hemagglutinin per strain), stimulating the older adult's immune system to provide higher antibody responses. [1]

A recent multi-center, randomized, double blind study compared high dose trivalent influenza vaccine to standard dose trivalent vaccine in adults 65 years or older during the 2011-12 and 2012-13 flu seasons. The study found laboratory confirmed influenza among 1.4% of those who received the high dose vaccination compared to 1.9% in the group that received the standard dose vaccine. The relative efficacy of the high dose vaccine was estimated at 24.2% (95% confidence interval, 9.7 to 36.5), and induced significantly higher antibody responses than the standard dose vaccine. Adverse effect rates were similar in both study arms, with 8.3% of those in the high dose group reporting adverse effects while 9.0% in the standard dose groups with a relative risk of 0.92 (95% confidence interval 0.85 to 0.99).[2] A subsequent analysis of Medicare claims data from 2012 to 2013 of patients greater than or equal to 65 years of age compared 929,730 recipients of the high-dose vaccine versus 1,615,545 recipients of the standard dose vaccine. The cohort analysis confirmed improved efficacy of the high-dose vaccine in influenza prevention in a real-world population. The high dose vaccine was 22% more effective than the standard dose vaccine for prevention of probable influenza infections and 22% more effective for the prevention of influenza hospital admissions.[3]

Table 1: FDA approved Influenza Vaccines 2015[1]

Product	FDA approved age	Inactive	Live	Trivalent	Quadrivalent	Special Considerations
Fluarix®	≥ 3 y	✓			✓	
FluLaval®	≥ 3 y	✓			✓	
Fluzone® (0.25mL)	6 – 35 months	✓			✓	For infants
Fluzone® (0.5 mL)	≥ 36 months	✓			✓	
Fluzone® Intradermal	18 – 64 y	✓			✓	Intradermal
Afluria®	≥ 9 y	✓		✓		
Afluria®	18 – 64 y	✓		✓		Needle-free, jet injector
Fluvirin®	≥ 4 y	✓		✓		
Fluzone®	≥ 6 months	✓		✓		
Flucelvax®	≥ 18 y	✓		✓		Egg-free, recombinant
Fluzone® High Dose	≥ 65 y	✓		✓		High Dose
FluBlok®	≥ 18 y	✓		✓		
FluMist®	2 – 49 y		✓		✓	Intranasal

While the effectiveness of the flu vaccine can vary from season to season, it is still important that all patients 6 months and older receive the flu vaccine every season.

Influenza Treatment

Since antivirals will only reduce sick time by one or two days, treatment is usually not recommended in otherwise healthy individuals, especially if symptom onset is greater than 48 hours prior to presentation. If antiviral therapy is indicated, it is most efficacious when initiated within 48 hours of symptom onset. Antiviral therapy has a greater role in populations that are at higher risk for more severe illness and associated complications such as pneumonia. Initiating therapy after the 48 hour window is still beneficial in more at-risk and severely ill populations.[4] These populations include individuals 65 and older, children younger than 5, pregnant women, and individuals with serious medical conditions including asthma, neurological and neurodevelopmental, blood disorders, chronic lung disease, diabetes, heart disease, liver disorders, metabolic disorders, morbid obesity, and those who are immunocompromised due to HIV/AIDS, cancer, or drug therapy.[4] The use of antivirals in these individuals will decrease the severity of illness, shorten the duration of the flu, and reduce the risk of complications and hospitalizations.

For the 2015-2016 flu season, the CDC recommends treatment with the neuraminidase inhibitor class of antivirals. These include oseltamivir (Tamiflu®), zanamivir (Relenza®), and peramivir (Rapivab®).[4]

Oseltamivir is one of the more familiar antiviral options used for both treatment and prophylaxis. It is approved for treatment of influenza in people who are 2 weeks and older and for prevention in those who are 3 months and older.[4,5] Current dosing recommendations are shown in Table 2, reflecting the most recent changes made to renal dosing in 2014. Treatment of influenza should be continued for 5 days while prophylaxis should be continued for 10 days.[4,5] Prophylaxis is most often recommended in high-risk individuals who have been directly exposed to the virus.

Oseltamivir is supplied in both pill and liquid form making it a preferable option for children. It also has the most study data on efficacy and safety in pregnancy so it is the preferred agent for pregnant women.[4,5]

Table 2. Treatment and Prophylaxis Dosing Recommendations.4-5

CrCl (ml/min)	Treatment	Prophylaxis
Normal and 61 - 90	75 mg twice daily	75 mg once daily
31 - 60	30 mg twice daily	30 mg once daily
11 - 30	30 mg once daily	30 mg every other day
≤10 and Hemodialysis	30 mg after each HD cycle	30 mg after alternate HD cycles
≤10 and Continuous Ambulatory Peritoneal Dialysis	A single 30 mg dose immediately after dialysis exchange	30 mg once weekly immediately after dialysis exchange

Zanamivir is another option for both influenza treatment and prophylaxis. It is formulated as an aerosol powder for inhalation that must be given via the DISKHALER inhalation device. It is approved for the treatment of influenza in people 7 years and older and for prevention in people 5 years and older. Due to its formulation, zanamivir should not be used in those with asthma, COPD, or other breathing problems.[4]

Peramivir was approved during the 2014-2015 flu season and is the first FDA approved intravenous option available for influenza treatment. It is currently approved for acute, uncomplicated influenza virus in people 18 years and older as a single 600 mg dose infused over 15 to 30 minutes. In one randomized-controlled trial, patients were randomized to receive peramivir IV 600 mg daily or placebo for 5 days. The median time to symptom resolution was 42.5 hours (95% CI, 34.0, 57.9) in the peramivir treatment group and 49.5 hours (95% CI, 40.0, 61.9) in the placebo group (P = 0.97) with the greatest effect seen in those patients who were started on peramivir treatment within 48 hours of symptom onset or were admitted to the ICU.[6] Reductions in viral shedding were greater in the peramivir treatment group. Despite these differences, peramivir was not found to be clinically beneficial in treating influenza in hospitalized patients and the study was terminated for futility.[6] Another phase III randomized, double-blind study compared one 600 mg dose of intravenous peramivir with a 5 day oral oseltamivir regimen. Peramivir was non-inferior to oseltamivir regarding time to alleviation of symptoms. The median times to resolution of symptoms were 78.0 hours (95% CI, 68.4, 88.6) in the peramivir group and 81.8 hours (95% CI, 73.2, 91.1) in the oseltamivir group. [7]

Advantages of peramivir include the availability of an intravenous option for severely ill patients without enteral access or concerns for adequate GI absorption. The main disadvantage of peramivir is its high cost in comparison to oseltamivir in addition to overall limited data demonstrating efficacy. A single 600 mg dose of peramivir is almost 8 times more expensive than a 5-day course of oseltamivir, and the study in hospitalized patients used five doses representing almost $5,000 per treatment course. Due to its noninferiority to oseltamivir and high cost, peramivir should be reserved for critically ill hospitalized patients without enteral access.

As the 2015-2016 influenza season kicks into high gear, remember the important role pharmacists play in the prevention of influenza via vaccination recommendation and administration, and prompt initiation of antiviral therapy for patients where influenza may be on the differential.

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"I am Your Pharmacist"

W. Arthur Purdum Award acceptance speech
by James Trovato, PharmD, MBA, BCOP, FASHP

For this evening I thought I would say a few words about my beliefs in the future direction of pharmacists' patient care in hospitals and health systems.

Eric Hoffer, an American writer, once stated that "The only way to predict the future is to have the power to shape it."

As a profession, I feel we can shape the future of pharmacists' patient care through the following steps.

We need to enhance our patients' and the public's understanding of the vital role of the pharmacist in their care.

When I first joined MSHP over 20 years ago, my first leadership opportunity was chairing the public affairs committee. Our goal was to increase awareness and educate the public about the pharmacy profession and role of the pharmacists in hospitals and other health systems. I encourage all of you to identify opportunities and ways pharmacists should educate the public, patients, and payors to enlist their support for availability of pharmacy care. We certainly do this through our advocacy initiatives, but the easiest way is to educate our patients when we encounter them in our practice sites. Patients need increased understanding of what pharmacists provide to improve medication outcomes, decrease adverse drug events, enhance safety and control the cost of their care. With this understanding, they will insist on access to the full services of pharmacists from employers and payers. Simultaneously, we should make the case to private and public payers that pharmacists will decrease health care costs, greatly expand access to care, and improve patient satisfaction.

"I am your Pharmacist"

How many times has a patient in the hospital, clinic, or other health system heard these words? Every patient that is admitted to the hospital should have a direct encounter with their pharmacist. It should be an expectation. As pharmacists, we all have a role to play in optimizing patient health and medication outcomes. If we don't, someone else will, and we cannot leave this role to other health care professionals. When it comes to advancing policy and procedures relating to the optimal, safe, and effective use of medications, pharmacy not only needs to be at the table, we need to be at the head of the table. Remember, if you are not at the table then you are on the menu!

Another step we need to take is to adopt an optimal practice model that defines important types and levels of patient care services provided by pharmacy and allows for application of best practices, standardization of care, and judgment of pharmacist and individual patient needs.

An Optimal Practice Model incorporates roles of pharmacists, technicians, and other support personnel into the provision of interprofessional care. Maximizing pharmacist's integration into health care teams will improve: Quality, Safety, Patient Satisfaction, and Financial Performance.

An optimal model encompasses patient care activities that span across all sites of care, including hospitals, clinics, home care, long term care, specialty pharmacy, community pharmacy, and urgent care and optimizes technology and information systems to enhance care and improve health outcomes for our patients.

We need to continue to identify and implement new methods of delivering patient care that eliminates pharmacists practicing in silos and focuses on the full continuum of medication therapy to improve outcomes of care and continue to strengthen effective transition of care mechanisms between these silos. Intraprofessional care is just as important as interprofessional. Pharmacists should collaborate in a coordinated fashion with pharmacists in different practice sites, including community pharmacy, to provide the full spectrum of patient care.

When I think about how pharmacists will function within new practice models, the term trans-professional comes to mind. Trans-professional is when the pharmacist takes on a role that is normally outside of his or her usual scope of practice but for which he or she does have the necessary base of expertise and teams up with the patient and/or family to provide care. I envision the development of trans-professional practice models that allow pharmacists to provide preventive care services, optimize and be accountable for patient health and medication outcomes, and receive reimbursement for cognitive-based services.

The future pharmacy practice model will become increasingly inter- and intra-professional and team-based; the vast majority of pharmacists' time will be spent providing direct patient care in all settings: medication preparation, distribution, & dispensing will be more centralized & automated and the technician workforce will provide more complex medication-use roles.

As you know, in the State of Maryland, many pharmacists are involved with medication therapy management (MTM) and collaborative drug therapy management (CDTM). I believe collaborative practice will evolve to include greater pharmacist responsibility for prescribing as part of coordinated health care teams in all settings. The current pharmacist prescribing model is vertical or top down where the pharmacist is dependent upon the physician.

We need to move to a horizontal or interdependent model where the physician makes the initial diagnosis and in specific patients and specific situations, previously determined by both the physician and the pharmacist, the pharmacist selects and designs a drug therapy regimen and writes the prescription or medication order.

Since this is a collaborative team based model, the pharmacist, along with the physician and nurse, review and monitor patient drug therapy for efficacy and adverse events. Subsequently, the pharmacist changes medication orders, consulting with the physician and nurse as needed. The goal is to improve patient outcomes, reduce costs, and make better use of physician, nurse, and pharmacist time.

Several key challenges and barriers, however, prevent the full integration of pharmacists into health care delivery teams. These include restrictive laws and regulations governing collaborative practice agreements. Pharmacist scope of practice is dictated by the laws and regulations in their state. Several states, including California, Montana, New Mexico, and North Carolina, have created the advanced practice pharmacy designation to expand pharmacist scope of practice through collaborative practice agreements. That designation allows pharmacists to provide direct patient care, including primary care.

The formal recognition of pharmacists as providers in state laws and regulations is a key step toward ensuring pharmacists serve as providers within accountable care organizations and other emerging models of team-based health care.

Going forward, pharmacists need to more fully participate in the design and provision of accountable care organizations (ACOs), identify and focus on high-risk patients, and measure the quality and financial impact of pharmacists on ACOs.

This is where your advocacy role becomes imperative on the state and national levels: for changes to expand pharmacist scope of practice and be recognized as providers. Pharmacists are the most accessible health care professionals and should be utilized as such to play a much larger role in primary care and the management of chronic disease.

In summary,

1. We need to educate the public as to the role of the pharmacist in patient care.
2. Pharmacists in different sites of care must work together to provide the full spectrum of care.
3. We need an increased emphasis on care basics, such as adherence, design of affordable drug therapies, elimination of unnecessary drug use, chronic disease management, wellness, and primary care.
4. There should be an increased pharmacy presence in clinics, medical homes, accountable care organizations, etc.
5. Finally, to achieve all of this pharmacy practice models must change significantly.

If you get the feeling that you are going under, staying focused on what is right for the patient will always be the best strategy. My name is Jim Trovato and I am your pharmacist!

Upcoming Board Meetings

- February 10 (Board only)
- March 9
- April 13 (Board only)
- May 11

A retrospective quality assurance analysis of pharmacist managed vancomycin therapy at a tertiary academic medical center

by Wesley D. Oliver, PharmD, Steven Gilmore, PharmD, BCOP, Asha Tata, PharmD, BCPS, and Brian Grover, PharmD, BCPS, University of Maryland Medical Center

Abstract

Purpose. Determine the percentage of patients achieving therapeutic vancomycin levels at 72 hours after the initiation of a consult to the pharmacist managed pharmacokinetic consult service.

Methods. A retrospective quality assurance analysis of 100 admissions from January 1st, 2014 to June 30th, 2014. Data analysis was performed using Microsoft Excel and included the use of descriptive statistics to summarize the demographic data, primary objective, and secondary objectives.

Results. For the primary objective, 78% of consults were able to achieve a therapeutic vancomycin level within 72 hours of initiation of the consult. At 72 hours, 13 patients had levels that were subtherapeutic and 6 patients had levels that were supratherapeutic. There were 5 patients that did not obtain therapeutic levels during the pharmacist consult. On average, pharmacists were able to achieve therapeutic vancomycin levels in 57.6 hours after initiation of a consult. A total of 11 patients experienced acute kidney injury after initiation of vancomycin. The average duration of the pharmacist managed consults was 7 days.

Conclusion. Overall, the pharmacist-based pharmacokinetic consult service successfully obtained therapeutic vancomycin levels in a majority of patients with a low rate nephrotoxicity.

Introduction

Vancomycin is a glycopeptide antibiotic that is the antibiotic of choice for the treatment of serious infections caused by gram-positive bacteria, particularly methicillin-resistant *Staphylococcus aureus*. It has a complex pharmacokinetic profile, with many factors, such as tissue distribution, protein-binding, renal function, and organism susceptibility, affecting the overall efficacy and safety of vancomycin.[1] These factors can vary tremendously between individual patients, making the dosing of vancomycin difficult.[1,2]

Due to the variability in patient-specific factors and susceptibility of microorganisms, current guidelines recommend monitoring steady-state vancomycin trough levels (before the fourth or fifth dose) to increase effectiveness and decrease the risk of adverse effects. Therapeutic vancomycin trough levels of vancomycin are between 10 mg/L and 20 mg/L depending on the site and type of infection, with more serious infections (e.g. pneumonia and CNS infections) requiring higher trough levels of 15 to 20 mg/L.[2,3] Vancomycin dosing guidelines recommend a trough level greater than 10 mg/L to prevent the development of resistance.[2] No causal relationship has been established, but higher vancomycin trough levels (ranging from higher than 15 mg/dL to higher than 30 mg/dL) have been associated with nephrotoxicity.[2]

It can be difficult for patients to achieve and maintain appropriate vancomycin levels due to patient variability, a narrow therapeutic index, and the risk of adverse events. However, it has been shown that pharmacist-managed therapy of narrow therapeutic index medications, including vancomycin, has been effective. In these studies, patients were more likely to reach and maintain therapeutic levels, have improved outcomes, and receive less costly care.[4-9]

The pharmacokinetic consult service at University of Maryland Medical Center (UMMC) was established in 2011 to provide therapeutic drug monitoring to inpatients. Medications managed by this service include vancomycin, aminoglycosides, warfarin, and various other medications with a narrow therapeutic index. The service is staffed by a weekly rotation of clinical pharmacy specialists, the majority completing two years of post-graduate training, and pharmacy residents. The service is staffed every day of the year and a pharmacist can be contacted 24 hours a day. An order for the consult service must be placed by the primary medical service. The consult service is then responsible for the management and monitoring of the medication. Assessment and adjustment of the therapy is expected within 24 hours and as frequently as clinically indicated thereafter. A quality assurance analysis has never been performed for the UMMC pharmacokinetic consult service. The purpose of this retrospective analysis was to determine the percentage of patients reaching therapeutic vancomycin levels at 72 hours after the initiation of a consult to the pharmacist managed pharmacokinetic consult service.

Methods

This study was a retrospective quality assurance analysis of 100 admissions from January 1st, 2014 to June 30th, 2014 with approval from the University of Maryland Institutional Review Board. The study included patients with vancomycin dosing consults to the pharmacokinetic service. Patients were excluded from the primary analysis if a non-consult provider modified the vancomycin therapy or the consult was discontinued prior to 72 hours.

The primary objective was to determine the percentage of patients reaching therapeutic vancomycin levels (10-20 mg/dL) at 72 hours after time of consult. The secondary objectives were time to achievement of therapeutic vancomycin levels after initiation of pharmacist consult, the number of vancomycin levels drawn after initiation of the pharmacokinetic consult, the percentage of patients with an increase in serum creatinine (50% rise from baseline) after initiation of vancomycin, and duration of pharmacist management.

Data was collected from the electronic databases utilized by our institution and included: age, gender, race, weight, comorbidities, assigned medical service, vancomycin indication, vancomycin level at 72 hours from initiation of consult, time to therapeutic vancomycin level, total number of levels drawn (by pharmacist and medical service) since initiation of vancomycin, baseline serum creatinine, peak serum creatinine during consult, and duration of pharmacokinetic consult.

Data analysis was performed using Microsoft Excel and included the use of descriptive statistics to summarize the demographic data, primary objective, and secondary objectives.

Results

The mean age of patients was 65 years old with more being male (51%) and white (61%). Patient comorbidities included hypertension (52%), diabetes mellitus (35%), and renal disease (18%). Most patients were admitted to a vascular or vascular surgery service (43%) and were receiving vancomycin for the treatment of skin and soft tissue infections (68%). (Table 1)

Table 1 - Demographic Variables.

Demographic Variables	**Value (n=100)**
Age (Mean, years)	65 (Range: 23-88)
Sex (%)	
Male	51
Female	49
Race (%)	
White	61
Black	34
Comorbidities (%)	
Hypertension	52
Diabetes Mellitus	35
Kidney Disease	18
Hemodialysis	9
Congestive Heart Failure	3
Chronic Liver Disease	2
Medical Service (%)	
Vascular/Vascular Surgery	43
Orthopedics	13
General Surgery	7
Surgical Oncology	6
Oral Maxillofacial Surgery	6
Other	25
Indication (%)	
Skin and Soft Tissue Infection	68
Osteomyelitis	7
Bacteremia	7
Sepsis	5
Respiratory Infection	5
Other	5

For the primary objective, 78% of consults were able to achieve a therapeutic vancomycin level within 72 hours of initiation of the consult. On average, pharmacist-managed consults achieved therapeutic levels in 58 hours with consults lasting 7 days. A total of 52 patients had levels drawn by the medical team, with an average of 1.6 levels per patient. Pharmacists ordered an average of 2.4 levels per patient for the 100 charts evaluated. A total of 11 patients experienced acute kidney injury after initiation of vancomycin. (Table 2)

Table 2 - Primary and Secondary Objectives.

Primary Objective	**Value (n=100)**
Patients reaching therapeutic vancomycin levels at 72 hours after time of consult (%) • Patients supratherapeutic (%) • Patients subtherapeutic (%)	78 6 13
Secondary Objectives	**Value (n=100)**
Time to achieve therapeutic vancomycin levels after initiation of pharmacist consult (Mean, Days)	2.4 (Range: 1-7)
Vancomycin levels drawn after initiation of pharmacist consult Pharmacist (Mean, #) Medical Service (Mean, #) Number of patients level drawn by medical service (#) • Average number of levels drawn by medical service (Mean, #)	 2.4 (Range: 0-7) 0.8 (Range: 0-7) 52 1.6 (Range: 1-7)
Patients with acute kidney injury after initiation of vancomycin (%)	11
Duration of pharmacist management (Mean, Days)	7 (Range: 3-22)

Discussion

Vancomycin is the most consulted medication for the pharmacist managed pharmacokinetic consult service at UMMC. The consult service was established based on anecdotal evidence that suggested units not covered by a clinical pharmacy specialist had difficulty with managing vancomycin therapy, potentially leading to inappropriate adjustments, suboptimal outcomes, or changes to more costly and broad-spectrum antibiotics. This service established extended clinical coverage with a targeted approach.

Medical services with clinical pharmacists already have vancomycin dosing and monitoring performed with pharmacist input; however, it may be beneficial to implement policies to allow all patients to have their vancomycin therapy managed by a pharmacist in order to maintain consistent practice. The outcomes of this analysis suggest safe and effective management using the methods described, but further study is needed to identify the percent of patients who have orders for a pharmacokinetic consult and how safety and efficacy in patients with pharmacist managed orders compare to patients without pharmacist managed orders.

Challenges encountered with the consult service include physician interruption of vancomycin dosing, ordering drug levels, and lack of communication with the consulting pharmacist. Our analysis showed that a majority of patients still had levels drawn by the medical service, approximately 2 levels per patient, and we excluded those patients who had adjustments made by non-consult providers. These levels not only increase the risk of a patient's vancomycin therapy being inappropriately managed but could also produce excessive, undue costs. Education and new policies added to the current practice model may enhance the orders and pharmacokinetic monitoring of vancomycin within the organization.

A small portion of patients in this analysis experienced acute kidney injury. The rate of injury is hard to compare to other studies since this is a quality assurance analysis and there are few similar studies in the literature; however, the rate in this analysis is lower than observed in a larger study.[4] It is important to note that from the data collected we cannot establish a causal relationship between vancomycin therapy and acute kidney injury, and the exact cause is likely multifactorial.

There are several limitations to this analysis. First, this was a retrospective quality assurance analysis with no comparator group, which limits the generalizability to other institutions or management by other providers. Second, there is no established benchmark for what is an acceptable percentage for our primary outcome. Similar results have been shown in projects discovered during the literature search; however, these studies were designed differently making comparisons difficult.[10,11] Lastly, we could not verify if the indications for vancomycin therapy were correct or if patients responded to therapy clinically. Thus, we are only able to assess the service's performance in managing vancomycin therapy and not patient outcomes.

Conclusion

Overall, the pharmacist-based pharmacokinetic consult service successfully obtained therapeutic vancomycin levels in a majority of patients within 3 days. Most patients had levels drawn by the medical service, which could have produced undue costs. A small percentage of patients experienced acute kidney injury; however, the exact cause is likely multifactorial and cannot specifically be determined.

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Pharmascript
Volume 40, Issue No. 1
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Call for Participation on the MSHP Pharmacy Technician Committee

The MSHP Pharmacy Technician Committee is seeking new members! The purpose of the Pharmacy Technician Committee is to enhance pharmacy technician awareness of and participation in MSHP. Current goals include addressing the educational and informational needs of pharmacy technician members of MSHP and providing a forum to facilitate communication, sharing of ideas and best practices related to pharmacy technician roles and responsibilities in health-system pharmacy. Attendance at committee meetings is facilitated through teleconferencing, and meetings occur at least once per quarter. Those interested in joining must be a member of MSHP and may be pharmacy technicians, student interns, or pharmacists. Current MSHP members are asked to encourage those who may be interested in helping to achieve the goals of the MSHP Pharmacy Technician Committee to consider membership!

Activities in which MSHP Pharmacy Technician Committee members may have the opportunity to be involved include:

- Identifying the needs of pharmacy technician members
- Planning and advertising pharmacy technician Continuing Education (CE) events
- Developing and soliciting pharmacy technician items of interest for the MSHP newsletter and/or the MSHP website
- Assisting with the selection of the Pharmacy Technician of the Year Award
- Providing education to pharmacy technicians about technician roles in the Practice Advancement Initiative
- Planning and participating in legislative activities to advance the role of pharmacy technicians

Current members of the MSHP Pharmacy Technician Committee are in the preliminary phases of planning a Pharmacy Technician CE and Networking Event for spring 2016. Tentative plans include providing 2-3 hours of CE, discussion of the benefits of MSHP membership, and time for socializing with fellow pharmacy technicians from across Maryland. If you are interested in joining the MSHP Pharmacy Technician Committee and/or would like to assist with planning the CE/Networking event, please contact the committee co-chairs, Stephanie Smith-Baker (sesmithbaker@aacc.edu) or Carla Gill (cgilla@jhmi.edu).

New Drug Update: Idarucizumab (Praxbind®)

by Katie Dane, Pharm.D. and Vi Gilmore, Pharm.D., BCPS, The Johns Hopkins Hospital

On October 16, 2015, the FDA approved Idarucizumab (Praxbind®) for use in dabigatran-treated patients requiring emergent surgery or urgent procedures, or experiencing life-threatening bleeding.[1] Despite the convenience associated with the use of direct oral anticoagulants compared to warfarin, the absence of a reversal strategy for patients receiving these medications plays a large role in the risk-benefit analysis employed in therapeutic decision making. The first FDA-approved agent of its kind, idarucizumab is a humanized monoclonal antibody fragment with high affinity for dabigatran, resulting in anticoagulation reversal.[2]

The medication was approved through the U.S. Food and Drug Administration's accelerated pathway based on the interim analysis results of the RE-VERSE AD Trial.[3] Idarucizumab was evaluated in the two groups of patients most likely to experience benefit from dabigatran reversal: patients with overt, uncontrollable, or life threatening bleeding and patients requiring invasive procedures that could not be delayed more than eight hours. Idarucizumab was administered to both groups as two 2.5 gram boluses separated by no less than 15

minutes. The primary endpoint, maximum percentage reversal of dabigatran determined four hours after administration of the second idarucizumab dose, was achieved in all patients enrolled. Tests of clotting activity normalized in 88-98% of patients, which correlated with an 80% reduction in serum dabigatran levels from peak concentrations. The median investigator-reported time to cessation of bleeding was 11.4 hours, while the median time to surgery was 1.7 hours from the first dose of idarucizumab. Thrombotic events occurred in five patients overall; however, none of these patients were anticoagulated at the time of the event. Due to observed increases in dabigatran levels 12 to 24 hours after administration, the utility of repeat doses of idarucizumab in certain populations should be evaluated in future studies.[3] While the results of the REVERSE-AD Trial are promising, additional data are needed to evaluate clinical outcomes with this agent. Moreover, the disparity between the rapid improvement in clotting parameters and time to cessation of bleeding in patients receiving idarucizumab must be further delineated.

Idarucizumab is available in cartons containing two 2.5 gram vials, for which the wholesale acquisition cost is currently $3,500 (verbal communication with Boehringer-Ingelheim, November 15, 2015).[2] The Institute for Safe Medication Practices urges facilities to consider the potential for look-alike sound-alike errors with idarucizumab and idarubucin, both of which require refrigeration.[4] Idarucizumab is stable for 48 hours at room temperature if stored in the supplied carton; however, once exposed to light the medication must be administered within six hours.[2]

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Rolapitant: A New Drug for Chemotherapy Induced Nausea and Vomiting

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Delayed chemotherapy-induced nausea and vomiting (CINV) develops in patients more than 24 to 120 hours after the start of chemotherapy and occurs commonly with the administration of cisplatin, carboplatin, cyclophosphamide, or doxorubicin.[1] Activation of the neurokinin (NK)-1 receptor plays an essential role in delayed CINV. Rolapitant (Varubi™) is a selective, orally available, long-acting NK-1 receptor antagonist. It was recently approved in September 2015 in combination with a 5-hydroxytryptamine-3 ($5\text{-}HT_3$) receptor antagonist and dexamethasone in adults for the prevention of delayed CINV associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) and highly emetogenic chemotherapy (HEC).[2] Currently, other available NK-1 receptor antagonists include aprepitant and fosaprepitant (prodrug of aprepitant).

Rolapitant was approved based on three multicenter, randomized, double-blind, phase III trials. The primary endpoint for these studies was complete response (CR), defined as no emesis or use of rescue medication in the delayed phase. Identically designed HEC-1 and HEC-2 trials compared the rolapitant regimen (rolapitant,

granisetron, and dexamethasone) with control therapy (placebo, granisetron, and dexamethasone) in patients receiving a chemotherapy regimen that included cisplatin >60 mg/m^2.[3] Treatment with rolapitant resulted in a significantly greater proportion of patients achieving a CR in the delayed phase compared with the placebo group (HEC-1: 73% vs. 58%, p <0.001; HEC-2: 70.1% vs. 61.9%, p=0.043).[3] Another phase III trial compared the rolapitant regimen with control therapy in patients receiving MEC regimens, with at least 50% of patients receiving a combination of anthracycline and cyclophosphamide. The CR in the rolapitant group (n=684) versus the placebo group (n=685) was 71.3% versus 61.6%, respectively (p <0.001).[4]

Possible adverse effects from this drug include neutropenia, hiccups, decreased appetite, and dizziness, but these reactions may be caused by combination therapy including 5-HT3 receptor antagonist and dexamethasone.

Rolapitant is available as a 90 mg tablet. The recommended dosage is 180 mg, approximately 1 to 2 hours before administration of MEC or HEC.[2] The half-life of rolapitant is approximately 7 days, which is significantly longer than aprepitant and fosaprepitant (9-13 hours). Since rolapitant is not an inhibitor or inducer of CYP3A4 like aprepitant and fosaprepitant, it has less potential for drug-drug interactions. However, rolapitant is a moderate CYP2D6 inhibitor, an inhibitor of Breast-Cancer-Resistance Protein, and an inhibitor of P-glycoprotein.[2] It is contraindicated with the use of thioridazine, a CYP2D6 substrate, as it may result in QT prolongation and Torsades de Pointes.[2] Precaution should be taken when given with other CYP2D6 substrates.

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New Drug Update: Isavuconazonium sulfate (Cresemba™)

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In March 2015, isavuconazonium sulfate (Cresemba™) was approved by the U.S. Food and Drug Administration for patients with invasive aspergillosis or invasive mucormycosis.[1] Isavuconazonium sulfate is the prodrug of isavuconazole and is the newest member of the azole antifungal class. Similar to other azoles, isavuconazole blocks the synthesis of ergosterol resulting in a weakened fungal cell membrane.
The efficacy of isavuconazonium sulfate for the treatment of invasive aspergillosis was demonstrated in a randomized, double-blind, non-inferiority, and multi-center trial with 516 patients.[2] The trial randomized patients 1:1 to isavuconazonium sulfate or voriconazole. Adults with probable or possible invasive fungal disease were included in the study. There was no difference in the primary endpoint of all-cause mortality through day 42 in the intent-to-treat population between isavuconazonium sulfate (18.6%) compared to voriconazole (20.2%).[2] There was also no difference in overall success rates (complete or partial response) between isavuconazonium (35%) and voriconazole (36.4%).[2]

The efficacy of isavuconazonium sulfate for the treatment of invasive mucormycosis was demonstrated in an open-label, multi-center, single arm trial with 37 patients.[2] Adults with proven or culture positive invasive fungal disease caused by molds, yeast or dimorphic fungi were included in the study. The primary endpoints were all-cause mortality through day 42 (37.8%) and day 84 (43.2%) and overall response (31.4%).[2] A case-control analysis using the Fungiscope Registry database led to the conclusion that isavuconazonium sulfate may be as effective as amphotericin-B based therapies for the treatment of invasive mucormycosis.[2]
Isavuconazonium sulfate is generally well tolerated. The most common side effects in both clinical trials were nausea (26%), vomiting (25%), diarrhea (22%), headache (17%), elevated liver enzymes (16%) and hypokalemia (14%).[3]

Isavuconazonium sulfate is available as a capsule and intravenous formulation.[1,3] The absolute bioavailability of the capsule is 98%, and each capsule contains 186 mg of isavuconazonium sulfate (100 mg of isavuconazole).[3] Treatment requires a loading dose of 372 mg every 8 hours for 6 doses, followed by a maintenance dose of 372 mg once daily starting 12 to 24 hours after the last loading dose.[3] It can be taken without regard to food.[3] Contraindications include familial short QT syndrome and concurrent use with strong CYP3A4 inhibitors or inducers.[3]

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New Drug Update: Secukinumab

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In January 2015, the FDA approved secukinumab (Cosentyx™) for treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.[1] Plaque psoriasis is an autoimmune inflammatory skin disease thought to be mediated primarily through interleukin (IL)-17A cytokine secretion, evidenced by elevated levels of IL-17A in psoriatic plaques.[2] Secukinumab binds to IL-17A and prevents downstream cytokine release.[1] It is the first IL-17A monoclonal antibody on the market.

Four double-blind placebo-controlled trials with a total of 2403 patients established the efficacy and safety of secukinumab.[1,3] The primary endpoints at week 12 of treatment included a 75% reduction in the Psoriasis Area and Severity Index (PASI 75) and treatment success, defined as "clear" or "almost clear" on the Investigator's Global Assessment (IGA). In all four trials, 75-87% of patients achieved PASI 75 and 62-73% achieved IGA treatment success.[3] The FIXTURE trial demonstrated the superiority of secukinumab 300 mg over etanercept for PASI 75 (77% versus 44%, $p<0.001$) and treatment success (63% versus 27%, $p<0.001$).[2]

Upper respiratory infections and diarrhea are the most common side effects of secukinumab.[1] Like other biologics, secukinumab can increase the risk of infections. Patients should be tested for tuberculosis before initiation. Secukinumab may also increase the risk of a Crohn's disease exacerbation and may cause hypersensitivity reactions.[3]

Secukinumab is prescribed commonly as a 300 mg self-administered subcutaneous injection to be given once weekly for five weeks followed by once every four weeks. The drug is available as a 150 mg prefilled syringe or Sensoready® Pen; therefore, patients may be required to administer two injections to achieve a 300 mg dose.[3] It must be stored under refrigeration and protected from light and agitation.

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