P&T Update

Formulary Addition/Deletion

Fulvestrant (Faslodex®) – formulary addition – approved

Fulvestrant (Faslodex®) is a competitive estrogen receptor antagonist FDA approved for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy. Request for formulary addition of fulvestrant was submitted by the Medical Oncology Division after review by the Oncology Subcommittee.

Chloral hydrate 500 mg/5 mL oral syrup – formulary deletion – approved

Motion was made to delete chloral hydrate 500 mg/5 mL oral syrup from the hospital formulary as the medication has been discontinued by all manufacturers.

Tigecycline (Tygacil®) – formulary addition – approved with restriction to ID

Tigecycline (Tygacil®) is the first of a new class of antibiotics called glycylcyclines. It is FDA approved for the treatment of skin and skin structure infections, community acquired pneumonia, and intra-abdominal infections. Formulary addition of tigecycline (Tygacil®) approved with restriction to ID.

Rosiglitazone (Avandia®) – formulary deletion – approved

Motion was made to delete rosiglitazone from the hospital formulary as the medication has been discontinued by all manufacturers.

Mebendazole (Vermox®) – formulary deletion – approved

Motion was made to delete mebendazole from the hospital formulary as the medication has been discontinued by all manufacturers.

Clevidipine (Cleviprex®) – formulary addition – approved, restricted to Anesthesia Department for OR use only.

Clevidipine (Cleviprex®) is a short-acting Calcium Channel Blocker (CCB) that was evaluated for addition to formulary. It is FDA approved for use in hypertension, perioperative hypertension, hypertensive urgency and emergency. Dr. Sergey, the requestor from anesthesia, appeared before the P&T Committee to answer questions regarding the use of this medication. He recommended adding this medication to formulary restricted to the OR, where its ability to be titrated is a key benefit over nicardipine. It was suggested that it should be restricted to neurosurgery procedures. The committee voted to approve the medication restricted to anesthesia use in the OR setting only. A one year review of the medication will be performed from the P&T approval date to assess the appropriateness of its usage and its continuation on the formulary.

Ranibizumab (Lucentis®) 0.3mg/0.05mL injection – Line of extension – approved

Lucentis® 0.3mg/0.05ml is a newer formulation of Lucentis® approved for use in diabetic macular edema. The cost is $1,170 compared to $1,950 for the current formulation (0.5mg/0.05ml). Motion was made to extend the product line for Ranibizumab to include 0.3mg/0.05mL dosage.
The FDA Approves REMS for ER and LA Opioids

On July 9th, 2012, the FDA approved the final Risk Evaluation and Mitigation Strategy (REMS) for extended-release (ER) and long-acting (LA) opioids. The goal of the new REMS is to ensure that health care practitioners are provided with the required information to dispense ER/LA opioids safely and to ensure that patients are supplied with information to safely use ER or LA opioids.\(^1\)

The content of the REMS was first announced in April 2011 as a measure by the Obama administration’s plan to decrease prescription drug abuse. The REMS incorporates a voluntary prescriber continuing education training program, which is financially supported by the manufacturers of the ER/LA opioid products.\(^1,2,3\) Knowledge, assessment and independent third-party audits will be required for the continuing education program content. The continuing education training program is expected to start on March 1, 2013. The FDA anticipates at least 60% of the U.S.’s ER/LA opioid prescribers will complete the voluntary training program in 3 years. A list of accredited education providers will be posted on www.ER-LA-opioidREMS.com. There are currently parts of legislation that are pending for mandatory continuing education training.\(^1\)

Furthermore, the REMS incorporates a patient education document for the prescriber to review with the patient, and a one-page Medication Guide (MedGuide) that is required to be dispensed with the LA or ER opioid to the patient.\(^1,2\) The new one-page MedGuide is also a new step for the FDA to improve all MedGuides. The new printed MedGuide for each product is not currently available; however, it will be available on the FDA’s MedGuide website.

Pharmacists are responsible to dispense the MedGuide to the patients of ER/ LA prescriptions.\(^1\) Pharmacists may benefit from using the prescribers’ patient counseling document and participating in the continuing education as well. This will allow the pharmacists to reduce risks and to safely provide medication for patients. The American Pharmacists Association is responsible for continuing its efforts to educate pharmacists regarding ER/LA opioids and pain management, abuse, misuse, and diversion.

The REMS has been brought together as part of a multi-agency federal effort, including the White House Office of National Drug Control Policy, the U.S. Department of Health & Human Services, FDA, and DEA.\(^1\) In order to reduce risk and improve safety, ER and LA opioid use must be controlled through education (REMS), monitoring, proper medication disposal, and enforcement. For more information, refer to the FDA’s website for a blueprint of the prescriber training program and a set of questions and answers.

References:

Contributed by:
Katherine Boutros, Pharm D. Candidate 2014, St. John’s University
New Pill Bottles for the Blind and Visually Impaired: A Vision for the Future

As of 2009, the National Eye Institute estimates that blindness and low vision affects about 3.3 million Americans ages 40 and over. By year 2020, they estimate that this number will rise to 5.5 million.1 According to the Department of Health and Human Services, age is considered to be the common factor that affects the accurate reading of prescription drug information and that only 30 percent of the geriatric population actually take their medications properly.1 With the increasing number of baby boomers reaching their 60s, not only will the geriatric population increase, but those suffering from blindness will too.5

The fine print on prescription labels can be difficult for the common patient to read. For the visually impaired, it can be a bit of a task, but for the blind it is completely impossible. More importantly, it can be potentially dangerous.1 Present pill bottles are hard to uncap, contain the package insert on a separate paper, and are inconveniently identical. Currently, there are a few options for the blind ranging from talking prescription bottles to Wi-fi connected light up systems. However, all prove to be expensive and technologically complex.3

Currently available is a Wi-fi connected prescription bottle with a cap that “glows” at the correct time to take a medication.3 Although this design seems practical, it proves to fail when there is no Wi-fi around and is only useful for those with limited sight. Another option is a radio frequency identification monitor known as RFID that provides an audio description of the medication when a bottle is passed over it. Also available, is an audio recorder system; however, this requires the pharmacist to manually record verbal instructions that are played back when the bottle is placed over the recorder.3 Another option is MedivoRx by Wizzard Software that adds a conversion of computer text into speech to a 1995 model of a talking prescription bottle. Although available in 8 different languages, this seemingly practical invention is only available in Illinois and New York.5 Despite the innovation of these current options, they prove to be intricate and require complex technology, as well as adding a cost burden. The RFID scripTalk device is about 200 dollars; however, the manufacturer does explain that they offer free patient units to those with “visual or print impairment” as part of their “Pharmacy Freedom Program”.2 Nonetheless, this system requires vocal recordings of the pharmacist and therefore may prove to be too time consuming.

Recently, two students from the University of Cincinnati developed a new design to benefit the blind and visually impaired that fulfills these shortcomings. This prototype prescription medicine pill bottle makes the identification and the use of the bottles more clear-cut and affordable. The two students, Alex Broerman and Ashley Ma, interviewed many patients and customers of existing products, and most “can't afford the time or money to learn these systems”.6 Thus, these technological devices remain out of reach for this population.4 Many of the patients have limited incomes and cannot afford “spending hundreds of dollars more than their sighted counterparts in order to aurally differentiate their medications”, explains Broerman.6 For those who cannot afford these costs, they continue to develop their own custom solutions; a rubber band around a specific bottle to discern it from others is an example.3 However, these solutions are temporary and do not go far enough to reach the needs of these patients to prevent medication errors.

Broerman and Ma have applied for a provisional patent on this innovation that could not only help those suffering from visual impairments from birth defects2, but also the cognitively impaired, illiterate, and elderly. This design consists of “hinged” lids that flip open which will significantly diminish the problem of lost caps- a problem that is substantially more dangerous for those with low vision.2,6 This feature also facilitates

(Continued on page 4)
New Pill Bottles for the Blind (Continued from page 3)

opening the bottle for elderly patients by eliminating the difficulty of twist caps, while remaining child proof. Also, this new bottle will be a small rectangular bottle, 2 by 2 inches wide and 3 inches tall with a “stout” design. This new shape will allow the patient to more conveniently reach in to pick out one or two pills. It eliminates the need to empty out all the pills into one’s palm to then selectively pick out the correct dosage. Simultaneously, it prevents the bottle from tipping over and spilling out the medication, which can be a danger to others. The design is available in eight distinct textured lids that can correspond to different medication. These textures are not Braille as one may think since only 10 percent of the visually impaired actually know and are able to read Braille. Each lid comes in a variety of deep colors to further distinguish each prescription bottle. Although this may not help those completely blind, older patients and those with limited sight are able to set apart strong colors. Finally, this new innovation contains a “fail-safe” audio button located on the lid that can be easily pressed to announce the medicinal contents of the bottle.

Unlike other models of the past and current options available, the key advantage to this design is that it involves simple technology and is inexpensive. Alex Broerman and Ashley Ma recently were recognized for their prototype and won a thousand dollar prize for their “Inclusive Pill Bottles for the Blind” in the 2012 “Innov8 for Health”; their design helps not only the blind and visually impaired, but has a universal appeal.

References:

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Influenza Vaccines

Influenza is a virus that causes respiratory disease, with symptoms of headache, fever, chills, sore throat, cough, muscle pain, and fatigue. It is usually mistaken for the common cold but can cause more serious consequences. Influenza can be spread through air by coughing or sneezing, or through contact with a contaminated surface. A person infected with influenza can be contagious as early as 24 hours before the start of any symptoms.

Certain populations are at increased risk of getting the flu and suffering from complications that could result in hospitalization. People at increased risk are the elderly, young children, and those with weakened immune systems. The more serious complications from the flu are ear infections, sinus infections, bronchitis, pneumonia, and sometimes death. The flu may also worsen certain condition; asthmatics may be more likely to suffer an asthma attack while they have the flu. Healthy people should get vaccinated in order to protect themselves as well as to protect others they come in contact with who might be more susceptible to getting the flu.

For the 2012-2013 flu season there are 6 manufacturers making the vaccine. The flu shot is usually given intramuscularly and contains an inactivated version of the influenza virus. Anyone aged 6 months and older can get the inactivated flu vaccine (TIV). The side effects of the inactivated vaccine are soreness and redness at the injection site.

An intradermal flu shot became available last year. It is also an inactive or killed version of influenza.
Influenza Vaccines (Continued from page 4)

Injection site is the skin, rather than the muscle, so the needle is 90% finer than the needle used for intramuscular flu shots. It is indicated for people 18 – 64 years old. The intradermal vaccine may also cause redness and soreness at the injection site. It can also cause headache, muscle ache, and tiredness, which last 3 – 7 days.³

Another option is a live intranasal influenza vaccine (LAIV). It works by prompting an immune response in a similar way that a real infection would. The intranasal vaccine is cold-adapted, meaning it replicates in the colder upper airways, like the mucosa of the nasopharynx and not in the lower airways. The live intranasal vaccine can be used in healthy people, 2 – 49 years of age. It is not for people with asthma, chronic medical conditions, or pregnant women. Healthcare workers and anyone who comes in contact with immunocompromised individuals should not get the intranasal vaccine. The intranasal vaccine may cause runny nose or nasal congestion.¹

The flu season typically ranges from October until March. It is recommended to get immunized as soon as the vaccine comes out in late summer although the vaccine remains available until the spring of the following year. It takes 2 weeks for the influenza vaccine to work after administration. Since the vaccines are made in fertilized chick eggs, it is contraindicated in people with severe allergic reaction to eggs.¹²

References:
2. Immunization Action Coalition & the National Influenza Vaccine Summit. 2012-2013 Influenza Vaccine Pocket Guide. Immunization Action Coalition & the National Influenza Vaccine Summit.

Contributed by:
Anila George, Pharm.D. Candidate 2014, Rutgers University

Dalfampridine (Ampyra®) Related Seizure-Risk

Dalfampridine is an oral potassium channel blocker approved by the FDA in 2010 to improve walking in patients with multiple sclerosis (MS). The ability to walk normally is often affected by this progressive inflammatory de-myelinating disorder.¹ In a randomized, double-blind, placebo-controlled trial, more patients responded to dalfampridine with a faster walking time in a timed 25-Foot Walk test. Although the mechanism of action is still unclear, one hypothesis involves dalfampridine’s effect on action potential transmission. Broad-spectrum inhibition of the Kv channel results in repolarization delay and prolongation of the action potential duration. This allows for a larger influx of Ca²⁺, thus increasing the efflux of neurotransmitters. The drug also directly triggers high-voltage activated Ca²⁺ channels independent of Kv channels.¹ In animals, dalfampridine has been shown to increase neuronal activity.²⁴

Possibly due to the broad-spectrum inhibition of potassium channels, seizures are one of the known side effects of dalfampridine and the risk increases with higher blood levels of the drug. FDA recently analyzed postmarketing case reports of seizures associated with dalfampridine at the labeled recommended dose.³ Of the 46,200 patients exposed, 85 seizures were reported as of March 31, 2011. This represents a seizure rate of 5.9/1000 patient-years of use. The mean age of the patients was 53 years (range, 15-76) and 78% of the reported cases were in women (66 women, 19 men). The duration of treatment prior to the event ranged from 1 dose to 365 days of treatment and 28% patients suffered a seizure within a week of starting treatment.³

In addition to the three-fold higher risk for seizures already inherent with MS, 61% of the reported cases had other confounding factors for seizure. Some of the confounding factors included: previous history of convulsion, renal impairment, dosing error (double dose or dosing interval less than 12 hours), use of concurrent medications with a labeled seizure risk, and head injury with a subdural hematoma prior to event. Of the patients experiencing seizures during dalfampridine therapy, 53% had concomitant use of

(Continued on page 6)
Dalfampridine (Ampyra®) related Seizure-Risk
(Continued from page 5)

one or more medications with a labeled seizure risk, 6% had a history of seizure, 4% had some level of renal impairment and 6% had an associated dosing error.\(^3\)

FDA is updating the dalfampridine drug label to clarify current recommendations that kidney function should be checked in patients before starting dalfampridine and monitored at least annually during treatment. Dalfampridine should not be used in patients with a history of seizures or who have moderate to severe renal impairment (CrCl <= 50 mL/min). For patients with mild renal impairment (CrCl 51-80 mL/min) the use of dalfampridine requires careful consideration of the potential benefits of treatment as well as the potential risk of seizure. Physicians should be aware of the age-related decreases in renal function, even if serum creatinine is normal. FDA warns that patients who miss a dose should not take extra doses, as an extra dose can increase the seizure risk. In addition, patients should take the tablets whole and avoid crushing, chewing or dissolving. Also, dalfampridine should be discontinued permanently if a seizure occurs. Physicians should also check for concomitant use of drugs with seizure risk.\(^5\)

In summary, the incidence of seizures on dalfampridine therapy during the one-year postmarketing period was similar to the incidence during clinical trials. In many of the cases, seizures occurred within one week of the start of dalfampridine therapy. Important findings from the case reports include the revelation of several confounding factors that increase seizure risk such as kidney function, previous history of convulsion, dosing error, and concurrent medication with a labeled seizure risk. FDA is updating the dalfampridine drug label to include warnings to safeguard against these confounding factors.

References:

Contributed by: Blessy George, Pharm. D. Candidate 2014, Rutgers, the State University of New Jersey

Insulin in the ICU

The role of insulin for blood sugar control in the Intensive Care Unit (ICU) has been a contentious topic for a number of years. There are two major approaches: intensive insulin therapy (IIT), where continuous insulin infusions are titrated to achieve normal physiologic blood sugar levels around 80-110mg/dL; and conventional insulin therapy (CIT), where higher blood sugar goals are targeted, usually around 140-180mg/dL. Since 2001, many trials, case reports, and meta-analyses have been published arguing for one side or the other. With the large volume of data regarding insulin use in the acute care setting and the conflicting nature of this data, it can be difficult to create an informed opinion. In this article, we will review the evidence and the guidelines regarding insulin therapy in the ICU.

This topic was first broached in 2001 by Van den Berghe and colleagues, who had an interesting question: Given that hyperglycemia can harm otherwise healthy patients over the long run, can it harm critically ill patients in the short run? To test this hypothesis, they randomized their hospital’s surgical ICU (SICU) population to receive CIT (targeting blood sugar levels of 180-210mg/dL) or IIT (targeting blood sugar levels of 80-110mg/dL). They discovered that in

(Continued on page 7)
Insulin in the ICU (Continued from page 6)

the IIT population, there was a marked decrease in mortality, from 8% to 4.6%. In the critical care setting, this result has enormous clinical significance; as the authors noted, “since the introduction of mechanical ventilation, few intensive care interventions have improved survival”.1

As such, the medical community was intrigued with this new concept of intensive insulin therapy and attempted to replicate Van den Berghe’s results. Given the impact of what had been discovered, many guidelines were revised to support IIT. However, the medical community was not blind to the shortcomings of Van den Berghe’s trial. Of particular concern was that his study only addressed the SICU population, which is quite different from the Medical ICU (MICU) population. To address this short-coming, Van den Berghe and colleagues published another study evaluating intensive insulin therapy in their MICU patients. While they found a decrease in morbidity in their IIT group, there was no difference between the CIT and IIT groups in mortality.2 Since then, many other trials were conducted, but none of them were able to replicate Van den Berghe’s original striking results, either in the number of patients included or the magnitude of the effect seen.

To attempt to settle the evidence regarding intensive insulin therapy, the NICE-SUGAR trial was designed, executed, and published in 2009. It was a multinational trial comparing the effect of IIT (blood sugar goals of 80-110mg/dL) versus CIT (blood sugar goals of 140-180mg/dL) in both MICU and SICU populations. Surprisingly, rather than finding no benefit, NICE-SUGAR’s results showed that mortality in the IIT group was higher than in the CIT group.3 At the same time, Griesdale and colleagues published a meta-analysis that evaluated all available evidence regarding insulin therapy in the ICU, including NICE-SUGAR’s results. Griesdale found that in SICU, but not MICU and mixed ICU populations, there was a mortality benefit from IIT.4 In these results, hypoglycemia is associated with increased mortality, and IIT is associated with increased rates of hypoglycemia. However, no causal relationship can be determined between the two and death. Further studies are currently underway to attempt to elucidate the mechanism by which hypoglycemia is linked to mortality.

In light of these results, the American Association of Clinical Endocrinologists and the American Diabetes Association jointly released a consensus statement in 2009 supporting blood sugar goals of 140-180mg/dL in critically ill patients.5 Most recently, ADA’s Standards of Medical Care in Diabetes 2012 reiterates their support of those blood sugar goals.6 The prevailing expert opinion is that while it is possible that there is a benefit from IIT, the literature has shown that this benefit is outweighed by the risk and consequences of hypoglycemia inherent in IIT.3-7

As we can see, Van den Berghe’s original question of whether or not hyperglycemia is harmful to critically ill patients remains unanswered. The evidence we have today indicates that there is limited clinical benefit to targeting normoglycemia. While we have been unable to rule out the possibility of a benefit from achieving normoglycemia in clinical studies, the increased incidence of hypoglycemia seems to negate and, in some cases, outweigh any potential benefit. The relationship between blood glucose levels and critical illness is an active avenue of research and will continue to be a focal point for research moving forward.

References:


Written by: Rakesh Babu, PharmD Candidate 2013, Rutgers, the State University of New Jersey
Metformin Promotes Neurogenesis by Activating a Specific Molecular Pathway

Recent research conducted in Canada and in the United States showed the possibility that metformin, a widely used drug for type 2 diabetes, might also play a role in the treatment of nervous system disorders. The research shows in a series of in vitro and in vivo studies that metformin recruits neural stem cells and enhances neural function. The possibility of metformin having a positive impact on the treatment of nervous system disorder is important since there is an increasing proportion of patients with both Alzheimer’s disease and diabetes, and hyperinsulinemia can speed the progression of neurodegeneration.

Metformin had been shown to activate AMPK and its downstream pathway, aPKC-CBP, in liver cells. Researchers began to hypothesize that meformin might also activate this pathway in neural stem cells; this pathway is needed for the development of embryonic neural precursor cells. In in vitro studies, nerve stem cells from both mice and human were cultured with metformin and successfully developed into mature brain nerve cells. In mice treated with metformin, the number of new neurons produced by stem cells nearly doubled, compared with controls, a difference that was significant (P<0.05). Twelve days of metformin treatment increased the number of new neurons by about 30% in the hippocampus, which is a region closely associated with new memory formation. In a key experiment with live mice in a water maze, the mice injected with 200 mg/kg of metformin for 38 days showed enhanced learning performance in the water maze when compared to the mice injected with saline alone. An earlier study conducted by Ohio University in 2006 had shown that metformin, given in doses in excess of those used in diabetes patients, could prolong survival in male transgenic mice with Huntington’s Disease. This study showed that metformin could cross the blood brain barrier, accumulate in the brain, and also increase brain AMPK activation.

Further research of metformin in other models of neurodegeneration is an important consideration since the ultimate mechanism of neurodegeneration in different diseases may involve common pathways. The results of these studies, however, show great promise in elucidating metformin’s potential role in the treatment of nervous system disorders.

References:


Contributed by:
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Tuberculosis: A Review on Resistance

Medical science has come a long way in the management of tuberculosis. Tuberculosis mortality has decreased 41% since 1990. The number of tuberculosis cases fell at a rate of 2.2% between 2010 and 2011. However, the global burden of tuberculosis remains high, with 8.7 million new cases reported in 2011.1

What’s worrisome is that there is an increasing incidence of multi-drug resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). MDR-TB is defined as patients who have a strain of Mycobacterium tuberculosis that is resistant to at least isoniazid (INH) and rifampicin (RMP). XDR-TB is defined as resistance to isoniazid, rifampicin, and one or more second line agents (quinolone class of antibiotics, streptomycin, capreomycin, kanamycin, or amikacin).2 This article will review the epidemiological trends and emerging therapies for MDR and XDR tuberculosis.

The World Health Organization published the WHO Global Tuberculosis Report 2012, which provides data on the epidemic and progress made in controlling the disease. Mortality among HIV-negative patients was almost 1 million deaths. The report indicated that the overall decline in tuberculosis incidence is too slow,

(Continued on page 9)
particularly in Europe and Africa. The number of MDR-TB cases has been increasing slowly (currently represents 3.7% of new cases and 20% of previously treated cases).¹ A recent epidemiology study by Dalton and colleagues found that MDR-TB and XDR-TB varies significantly between countries (Eastern Europe, Peru and Southeast Asia). The study found that the strongest risk factor for MDR-TB was previous treatment with second line agents. The study concluded that prevalence of resistance to second line drugs among pulmonary MDR-TB isolates is very high at 43.7% and risk of XDR-TB was 6.7%.²

Current guidelines for the management of tuberculosis from the World Health Organization state that there is no known “effective regimen” for isoniazid-resistant patients.³ As MDR pathogens are becoming increasingly resistant to second and third line agents, different classes of antibiotics are being studied and have shown promise. A recent randomized study was conducted in Korea, which examined the use of linezolid (an oxazolidinone class antibiotic) in patients with chronic XDR-TB.⁴ Although the study was small (total of 39 patients), the results showed that use of linezolid, along with the existing regimen that the patient was using, resulted in sputum culture conversion at a median time of 75 days for 89% of patients.⁴ Another study looked at the use of a new agent, delamanid, for patients with MDR-TB. Patients were randomized to three groups: 100mg delamanid BID plus background regimen, 200mg delamanid BID plus background regimen or placebo plus background regimen. The study concluded that more patients had sputum conversion at two months in the delamanid groups versus placebo group (45.4% in the 100mg delamanid group, 41.9% in the 200mg delamanid group and 29.6% in the placebo group).⁵

Although, emerging strains of tuberculosis are becoming harder to treat, the overall mortality rate for tuberculosis has decreased worldwide. Patient compliance is a major barrier in managing tuberculosis and a major reason for emergence of resistant strains. As pharmacists, it is important to make sure patients are staying compliant and they finish their full treatment course with their medications to avoid resistance.

References:

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Aminoglycoside Dosing: A Pharmacist’s Guide

Pharmacokinetics is an important science when it comes to individualizing drug therapy. Patient-specific dosing recommendations greatly increase efficacy and decrease toxicity from many medications. Aminoglycoside therapy is just one of the many different types of drug therapies that utilize pharmacokinetics to produce serum drug concentrations that result in beneficial pharmacologic effects while avoiding adverse effects. Aminoglycosides exhibit concentration-dependent killing; they work best when the peak serum concentration is as high as possible above the minimum inhibitory concentration (MIC), the lowest concentration of antibiotic necessary to inhibit bacterial growth. Notable adverse effects that apply to aminoglycosides include nephrotoxicity, which is associated with high trough plasma levels, and ototoxicity, which is associated with high peak plasma levels. Due to the variability seen among individual patients given these medications, it is necessary to take patient-specific factors into account when calculating the optimal dose.

There are several methods available to calculate the appropriate dosing regimen for a patient with normal renal function. The preferred method of aminoglycoside dosing is once-daily dosing using the Hartford Nomogram. To use this method, the patient’s serum drug level is checked about 8 hours after giving an initial dose of 7 mg/kg for gentamicin and tobramycin or 15 mg/kg for amikacin. It is important to note that if the patient is obese (20% over their ideal body weight), their adjusted body weight should be calculated and used to determine their initial dose. The formulas for ideal body weight (IBW) and adjusted body weight are provided below. The nomogram in Figure 1 is then applied using the serum level and time of blood draw to determine the dosing interval. Be sure to divide the plasma level by 2 first when using the graph for amikacin.

\[
\begin{align*}
\text{IBW}_{\text{males}} (kg) &= 50 + 2.3 \times (Ht - 60) \\
\text{IBW}_{\text{females}} (kg) &= 45 + 2.3 \times (Ht - 60) \\
\text{Adjusted body weight (kg)} &= \text{IBW} + 0.4 \times (Wt - \text{IBW}) \\
Ht &= \text{height (in)} \\
Wt &= \text{weight (kg)}
\end{align*}
\]

Figure 1: Hartford Nomogram

Another option is to monitor trough levels ½ - 1 hour before the next dose for once daily dosing of aminoglycosides.

<table>
<thead>
<tr>
<th>Once Daily Aminoglycoside Dose</th>
<th>Target Trough (mcg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin 7mg/kg q24h</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Tobramycin 7mg/kg q24h</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Amikacin 15-20mg/kg q24h</td>
<td>&lt; 4-5</td>
</tr>
</tbody>
</table>

* Use adjusted body weight for dosing if patient is obese (i.e. > 20% over the ideal body weight)

** This dosing is for normal renal function

Traditional empiric dosing is another method of designing a dosing regimen. Using this method, the patient is given a set dose every 8 or 12 hours. The recommended dosing ranges are listed below for patients with normal renal function.

(Continued on page 11)
Aminoglycoside Dosing: A Pharmacist’s Guide
(Continued from page 10)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>1.5 – 2 mg/kg q8h</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1.5 – 2 mg/kg q8h</td>
</tr>
<tr>
<td>Amikacin</td>
<td>5 mg/kg q8h or 7.5 mg/kg q12h</td>
</tr>
</tbody>
</table>

It is important to monitor the patient’s peak and trough levels to avoid ototoxicity and nephrotoxicity. For amikacin, gentamicin, and tobramycin, the peak needs to be sampled 30 minutes after the end of a 30-minute infusion or immediately after a 1-hour infusion. The trough should be sampled 30 minutes before the next dose. This would ideally be done when the drug levels have reached steady state after 3 to 4 doses. The recommended ranges for amikacin are 20 – 30 mcg/mL for peaks and < 8 mcg/mL for troughs. For gentamicin and tobramycin, the peaks should fall within 5 – 10 mcg/mL and the troughs should be < 2 mcg/mL.

Understanding how these medications combat pathogens helps to determine how the medications should be dosed. However, regardless of which dosing method is used, it is important to ensure that the patient’s serum levels fall within the recommended ranges. Going too far above the range puts the patient at risk for ototoxicity and nephrotoxicity and going below would allow the infection to persist and worsen. Keeping the serum drug levels within the therapeutic ranges requires careful vigilance and therapeutic drug monitoring to ensure the best therapy for patients.

References:

Written by:
Rozena Varghese, PharmD Candidate 2013, Rutgers, the State University of New Jersey

UH Adult Code Cart Update:

Once the new ACLS guidelines by AHA became available, Pharmacy Dept. set out to revamp the adult code carts as a part of continued quality assurance and performance improvement. The adult code cart content list was revised after input from multiple disciplines including Cardiology, Surgery and Anesthesia. The key changes included: revised code medications as per the new ACLS guidelines, availability of ready to use medication formulations per ISMP advisory, inclusion of laminated AHA/ACLS handouts, medication dosing/mixing/titration sheets and medication content layout schematics to be hung outside the carts. This revised list was approved by the Combined Critical Care Committee, the P&T Committee, the Code Blue PI Committee and the Medical Executive Committee. Pharmacy Dept. in collaboration with material management physically finished updating 59 adults carts this year which are fully operational now. These carts are constantly checked and maintained as per the Code Cart Check policy.

Contributed by:
Nishat Faruqui, Pharm D, Clinical Pharmacy Specialist
On November 28, 2012, many middle school students gathered at the Pharmacy Department to learn about the different careers available in healthcare at UMDNJ. This event, involving Citizen Schools Program of the Newark Early College High School was coordinated by Stacie J. Newton, MPA, Director of Marketing Communications, Dr. George Sienkiewicz, PhD. Pfizer Inc., and Mr. Andre Emont, MS, RPh, Director of Pharmaceutical Division.

When the students arrived, Mr. Emont launched the career program with opening remarks, and the field trip began with introductions from the representative clinical pharmacists and staff pharmacists. One by one, the students also introduced themselves and what they wanted to become in the near future. Our clinical pharmacists and staff pharmacists gave a brief overview of their job responsibilities and provided a little taste of what they do, grabbing the attention and interest of all the students.

Mr. Emont also explained doctor of pharmacy (Pharm.D.) program entry requirements and average salaries for pharmacists. Under the direction of Mr. Emont, Mr. Pardo, Dr. Jen, Dr. Faruqui, Dr. Punnoose, and Dr. Chu, the students were very excited about the opportunity to visit UMDNJ-University Hospital and tour the pharmacy. Overall, the career field trip was a great success as it provided some guidance to the students on their way to a bright, successful potential future in the healthcare field.

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