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Albany College of Pharmacy and Health Sciences

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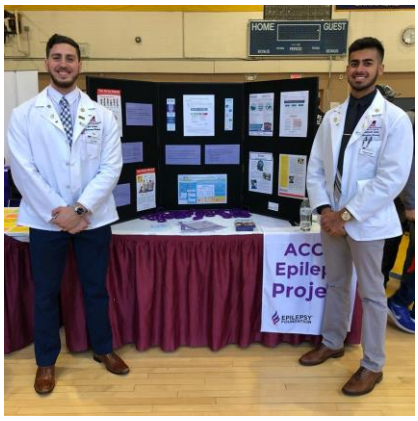
ACPHS-SCCP Student Chapter Update

Albany College of Pharmacy and Health Sciences' (ACPHS) SCCP chapter's mission is to promote early involvement in the American College of Clinical Pharmacy (ACCP) as a national organization. Since our chapter was founded, students have been given the opportunity to develop and display clinical knowledge, hands on skills, and professionalism to prepare them for future endeavors as pharmacy professionals. With the aid of our faculty advisors, Dr. Kate Cabral and Dr. Michael Kane, ACPHS-SCCP focuses on providing networking, clinical experience, and direct patient care opportunities for our members.

Our patient care projects promote education and awareness in the community, which are the main goals in the Script your Future and Epilepsy projects. Additionally, these projects expose SCCP members to various areas of clinical pharmacy, seen in our Cardiovascular and Renal (CaRE) screenings and CaRE for KIDneys projects.

The Script Your Future (SYF) project emphasizes medication adherence in various settings. Members have attended an English as a Second Language class and an HIV/AIDS resource center, where they cleared up any discrepancies and offered tips for complicated medication regimens. Last year, SYF attended the Washington Park Lakehouse's annual AIDS Walk here in Albany. Members and volunteers helped patients fill out wallet medication cards, gave away pill boxes, and counselled patients on the importance of medication adherence. Our growing Epilepsy project advocates for the understanding of what epilepsy truly is and how it affects the lives of those afflicted. Last year, they raised awareness and educated students by screening a movie about epilepsy on campus.



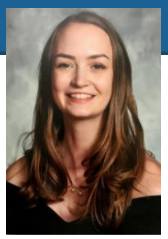
Our chapter's CaRE screenings give members and students a unique opportunity for hands on experience. After going through training, volunteers have completed screenings in senior housin g, churches, YMCAs, and on Legislative Day at Albany's Capital Building. Participants measured blood glucose levels and blood pressure and counselled patients about their results. CaRE for KIDneys visits elementary schools in the Albany area to educate and enhance curiosity in the science field. At our last event, DNA was extracted from strawberries and children were taught basic genetics.

Members and students at ACPHS may also benefit from attending any of our Clinical Pharmacy Challenges. We host six of these challenges per year. Each challenge is based on a clinical topic such as nephrology, neurology, and cardiology. Attendees compete by answering Kahoot! questions for prizes.

Each of our patient care projects are hard at work planning and organizing events for this year as we continue to expose and educate students on the growing world of clinical pharmacy. We have a large following of active students that are eager to get involved and participate in our events. With growing interest and new event ideas, we look forward to seeing what our organization will do in the future.

Colin Duell, PharmD Candidate ACPHS Class of 2022

Clinical Spotlight: Emily Valentine, PharmD, PGY-1 Resident at Salem VA Medical Center



Interviewed by Karly Smerkar, PharmD Candidate, ACPHS Class of 2020

Why did you choose to pursue a residency?

I decided to do a residency because I wanted to be able to apply the skills and knowledge I gained in school in a clinical setting. I enjoy being a valued member of the healthcare team and practicing at the top of my license. I knew that doing a residency was the best way to prepare myself for a career that allows me to do those things.

What made you want to pursue a residency at the VA?

I first learned about the VA when I participated in the VA Learning Opportunities Residency (VALOR) program at the Albany VA Medical Center during my P2 and P3 year. The neat thing about the VA is that clinical pharmacy specialists are providers with their own scope of practice. Patients are

referred to a clinical pharmacy specialist by their physician and then the patient makes appointments to see us where we initiate, discontinue, or adjust medications as well as order labs under our own name. Plus, the veterans are amazing people and it's such an honor to be able to serve those who served us.

How would you describe a typical work day for you?

Busy, but exciting! The specifics of my day depend on what rotation I'm on. Right now, I'm on an internal medicine rotation. In the morning, I work up my patients for the day and discuss them with my preceptor. I let her know of any suggestions I want to bring up to the medical team. Then I go on rounds with the team (usually by myself), where I make suggestions and the medical residents ask me questions. After rounds, I let my preceptor know what happened during rounds and then head back to my desk to write up notes on the patients or follow-up with any questions the team asked me during rounds. There are also plenty of meetings, conferences, presentations, and topic discussions to attend throughout the week. Once a week, when my day at rotation is over, I head over to the inpatient or the outpatient pharmacy to staff for a few hours. I'm pretty much always busy, but it's very rewarding.

What tools or resources do you currently utilize to expand your clinical knowledge or skills?

Through the VA, I attend a lot of things like journal clubs, webinars, CEs, and grand rounds which help keep me up to date. I also like to read the Pharmacy Times emails to keep up with what's new in pharmacy.

What has been your greatest challenge in your pharmacy career thus far? How did you overcome it?

My biggest challenge so far was during my P3 year when my mom got very sick and passed away. During that time, I drove 3 hours each way almost every weekend to go home and be with my family. It was a challenge to balance family, work, school, clubs, professional organizations, and a social life. During that time, I leaned very hard on my family and friends. I learned that
when you're overwhelmed and have a lot of things to balance, it's important to take things one day at a time and really prioritize what needs to be done first and what isn't so important.

Describe your growth as a pharmacist since starting your residency

Even though it has only been a few months, I have already grown a lot as a pharmacist. A lot more is expected of you as a resident than a student. There is a lot of responsibility, but it's helping me to gain a lot of clinical knowledge as well as helping me learn how to communicate with patients and other providers. When I'm staffing on evenings and weekends, I am fully independent, which was a little nerve-wracking at first, but is allowing me to gain confidence in my skills and abilities.

What advice do you have for students who are interested in pursuing a residency?

Two things: keep an open mind and be yourself. It's important to have a clear goal and vision for your future, but not to commit yourself to one thing. You may find somewhere or something you never thought you would like, so it's good to be open. It's important to be yourself because you will be more relaxed and will appear genuine. Plus, if a program doesn't like the real you, then it's not a program you want to be at!

Update on Prevention Early-onset Group B Streptococcus Infection in Newborns – Revised Recommendations by American College of Obstetrician and Gynecologists

By Merihan Raouf, PharmD Candidate, ACPHS Class of 2020

Early-onset group B streptococcus (GBS) is considered the leading cause of infection in newborns. GBS is an encapsulated gram-positive coccus that colonizes the gastrointestinal and genital tracts of 15 – 40% of pregnant women. About 50% of women colonized with GBS will transmit the bacteria to their newborn, through vertical transmission. Vertical transmission usually occurs during labor or after the rupture of membranes, which results in early-onset disease in neonates. It is recommended to begin intrapartum antibiotic prophylaxis in women at risk of vertical transmission to prevent newborns from contracting the bacteria.

In July 2019, the American College of Obstetricians and Gynecologists (ACOG) released updated guidelines for prevention of GBS infection in newborns. These guidelines include information regarding screening and

prophylactic treatment recommendations. Screening involves routine rectovaginal GBS cultures and correct specimen collection to assess potential risk. Gynecologists recommend performing screenings between 36 0/7 and 37 6/7 weeks of gestation. Women undergoing planned caesarian section prior to labor onset and with intact membranes are considered low risk and thus, are not candidates for intrapartum antibiotic prophylaxis. Intrapartum antimicrobial therapy should be administered to women with positive cultures for GBS and planning a natural birth. In the circumstance that high risk women experience the onset of labor before cultures are known, antimicrobial therapy is recommended. Antimicrobial therapy is also indicated in women with positive GBS colonization in prior pregnancies even if there is no current culture or unknown culture results. The mainstay of therapy remains intravenous penicillin G (5 million units initially, then 2.5-3 million units every 4 hours until delivery). If penicillin allergy is present with a low or unknown risk of anaphylaxis, cephalosporins (e.g., cefazolin) are considered an adequate alternative. If women are at high risk of anaphylaxis to a cephalosporin, clindamycin is recommended only if bacterial susceptibility is confirmed. If culture results are not available or if the culture is not sensitive to clindamycin, intravenous vancomycin is recommended. The updated guidelines further define vancomycin dosing to be based on weight and renal function; 20mg/kg intravenously every 8 hours, with a maximum of 2g per single dose in patients with normal renal function. Monitoring of renal function is also important with vancomycin dosing due to the risk of nephrotoxicity. Finally, treatment with antibiotics antepartum should be avoided as it does not lower the incidence of GBS colonization at the time of delivery.

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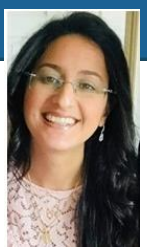
A New Approval: Tafamidis (Vyndaqel) for the Treatment of Transthyretin Amyloid Cardiomyopathy



By Maryam Yassa, PharmD Candidate, ACPHS Class of 2020

Tafamidis (Vyndaqel), an oral selective stabilizer of transthyretin, was recently approved in May of 2019 as the first FDA-approved treatment made to target symptomatic transthyretin (TTR) amyloid cardiomyopathy. Based on the results of the ATTR-ACT randomized, placebo-controlled trial, tafamidis appears to provide a promising, new mechanism of action in the treatment of ATTR amyloidosis.

Transthyretin is a tetrameric transport protein found in the cerebrospinal fluid and serum responsible for transporting retinol (vitamin A), and to a lesser extent, thyroxine. Various transthyretin gene mutations exist which increase the rate of tetramer dissociation into monomers, which are subsequently able to misfold and form amyloid fibrils.[1] Transthyretin amyloid cardiomyopathy is a rare, life-threatening condition in which transthyretin amyloid fibrils deposit in the heart tissue.[2] Another form of transthyretin amyloidosis exists; transthyretin familial amyloid neuropathy, in which the fibrils mainly affect the peripheral nerves. Treatment of TTR cardiac amyloidosis, per the American Heart Association's scientific statement on Current Diagnostic and Treatment Strategies for Specific Dilated Cardiomyopathies, mainly consists in symptomatic management.[2] The mainstay of heart failure management remains diuretic use. ACE inhibitors and ARBs should be avoided due to hypotension risk in cardiomyopathy. In the setting of atrial fibrillation, heart rate can be controlled with beta blockers, although they are better avoided in amyloidosis.[2] One trial found benefit with the use of diflunisal (Dolobid) in increasing TTR stability, but it is not approved for use in TTR cardiomyopathy. Its use may also not be ideal due to the risks associated with chronic NSAID use.[3] Other treatment options include liver or heart transplants, which, due to many factors including advanced age, need for lifelong immunosuppression, and surgical risk, may not make them an ideal treatment option.[3,4]

The rationale behind the use of tafamidis in TTR cardiomyopathy is to prevent the dissociation of the transthyretin tetramer, thus stabilizing the tetrameric form of transthyretin by increasing the activation barrier. Phase 3 of the ATTR-ACT international, multicenter, double-blind, placebo-controlled, randomized clinical trial that began in December to 2013 and was completed in February 2018 had the purpose of evaluating the efficacy, safety and tolerability of daily oral tafamidis dosed at 20mg or 80mg compared to placebo in patients diagnosed with transthyretin cardiomyopathy. Patients were included if they were between the ages of 18-90 years old and had TTR cardiomyopathy, or if they did not have TTR cardiomyopathy but had the presence of the transthyretin precursor protein, confirmed through immunohistochemical analysis, scintigraphy and mass spectrometry. To confirm cardiac involvement, ECHO, septal wall thickness greater than 12mm, history of heart failure, prior hospitalization due to heart failure, or clinical manifestations of heart failure without hospitalizations were used as determinants of such. Exclusion criteria consisted in: heart failure not attributable to TTR, NYHA class IV heart failure, light chain amyloidosis, patients with a heart or liver transplant, a cardiac implanted device, previous treatment with tafamidis, concurrent treatment with NSAIDs, digitalis, calcium channel blockers, doxycycline, tauoursode-oxycholate, a GFR less than 25mL/min, liver transaminases greater than two times the ULN, and cases of severe malnutrition defined by a modified BMI of less than 600.

The primary outcome measure was the hierarchal combination of all-cause mortality and frequency of cardiovascular-related hospitalizations, analyzed over the 30-month trial period. Secondary outcome measures were the percentage of patients with stabilized TTR at 1 month, number of participants with cardiovascular-related mortality, all-cause mortality, frequency of cardiovascular-related hospitalizations
from baseline to month 30, change from baseline in the total distance walked during the 6 minute walk test (6MWT) at month 30, and the change from baseline in KCCQ-OS at month 30.

A total of 441 participants were randomized to one of three arms: tafamidis 20mg once daily, tafamidis 80mg once daily or placebo in a 2:1:2 ratio, respectively. Those receiving the 80mg dose had the option of reducing the dose to 40mg during the trial if they experienced adverse events that may have influenced adherence or continuation of participation in the trial.[3]

Characteristics at baseline between tafamidis and placebo groups were comparable, most patients being male and median age being 75.[3] The male: female gender ratio of ATTR transthyretin amyloidosis is 9:1.[5] The primary Finkelstein-Schoenfeld analysis showed evidence that use of tafamidis was superior to placebo over the 30 month period ($p<0.001$). The win ratio was 1.695 (95%CI 1.255 -2.289). All-cause mortality was lower with tafamidis than with placebo per Cox regression analysis (29.5% vs 42.9%; hazard ratio 0.7, CI 0.51- 0/96). Poisson regression analysis showed that the rate of cardiovascular-related hospitalizations was less with tafamidis treatment as compared to placebo (RRR 0.68, CI 0.56- 0.81). All-cause mortality was decreased with tafamidis treatment, as was seen per analysis of Kaplan-Meier survival curves, with differences seen at around 18 months of treatment. The only case in which cardiovascular-related hospitalizations were higher in the tafamidis arm was in patients with NYHA class III at baseline. This was likely attributable to increased survival times during more severe phases of illness.[3]

Compared to other trials or to previous treatments, tafamidis is the first approved medication that will in fact target transthyretin amyloid fibrils and stabilize them in their tetrameric form to prevent dissociation, and thus prevent aggregation in cardiac tissue. This is different from the current mainstay which consists mainly in symptomatic management of heart failure, in the hopes that more targeted therapy will improve outcomes.

A limitation of this study was that it only assessed safety and efficacy over a 30 month period, and so the long term effects of this novel medication are not yet known. This study also did not provide a duration of time for which tafamidis should be used; it only revealed that its use was of benefit over a 30-month period. In addition, the trial does not specify at which time in the course of a patient's disease at which tafamidis should be initiated or in which it would be of most benefit, or if its use should be long term.

In conclusion, tafamidis is the first FDA-approved medication to target the pathophysiological TTR fibrils that result in TTR cardiomyopathy. At both 20mg and 80mg doses, tafamidis showed a decrease in all-cause mortality, cardiovascular-related hospitalizations, and a slower decline in quality of life based on its use over a 30-month trial period compared to placebo. Long-term effects have not been studied and are not known at this

time, and the duration of use and point of time in one's disease course at which tafamidis should be used were factors that were not addressed by the ATTR-ACT trial. Nonetheless, the targeted mechanism of action of this novel medication does appear to provide promising outcomes for TTR cardiac amyloidosis patients.

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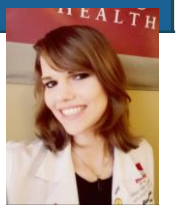
Management of Candidiasis (Candidemia, Thrush, and the Microbiome)



By Allison Gorseth, PharmD Candidate, ACPHS Class of 2020

Candidiasis refers to fungal infection which is primarily caused by one of 15 common Candida species.[1] In clinical practice, it is recommended to guide the treatment of Candida infection based on the site of the infection, as well as the species of Candida present. Since Candida is part of the normal flora in the mouth, throat, gut, and genitourinary tracts, it is not always necessary to treat positive sputum or urine cultures since it may be reflective of the patient's normal microbiome.[1,2]

Healthy patients can contract a Candida "infection" in the back of their throat or mouth, commonly called oral thrush.[2] Oral thrush is caused by the overgrowth of C. albicans. It is usually an asymptomatic accumulation of white lesions for healthy individuals, but for patients with reduced immunity the symptoms can become more severe including difficulty eating or swallowing, loss of taste, and extension of lesions involving the esophagus.[1,2] If this occurs, it can make food difficult to swallow, potentially causing choking or malnutrition. Medications associated with increasing a person's potential of oral thrush include antibiotics and steroids (inhaled or systemic).[2] Additionally, uncontrolled diabetes will cause an increased about of sugar in saliva which gives the candida fuel to grow. [1,2] To treat thrush, various treatment options can be used depending on the setting. For outpatient therapy, clotrimazole 10mg lozenges or nystatin 400,000-600,000 units four times daily is recommended. For inpatient therapy, chlorhexidine washes or fluconazole therapy can be considered to reduce the risk to esophageal progression.[2]

Blood is a sterile site of the body. Candida in the blood is referred to as candidemia and makes up of 40% of bloodstream infections in the nosocomial setting.[2,3] It is the 4th most common cause of bloodstream infections.[3] Risk factors include immunodeficiency, diabetes, use of corticosteroids or broad spectrum antibiotics, placement of a central line, and residence in the intensive care unit (ICU).[2] The infection usually develops within the first week in high risk patients admitted to the ICU.[3] Identification of candidemia can also be difficult due to the non-specific signs and symptoms of the disease including fever, chills, generalized weakness, fatigue, headache and neurological changes.[1] A fungal infection spreading to the organs of the body from the bloodstream, is referred to as invasive candidemia. Common organs initially involved include the liver, kidneys, and eyes.[2,5]

Source control is vital to sustained, effective candidemia treatment. If the source of the spread of candida through the body can be pinpointed, the source needs to be isolated and removed (e.g., removing a contaminated central line). Source control allows the infection to be eradicated. Antifungals can be initiated before source removal, but the fungal infection will recur if the origin is not remedied. In order to select the correct medication, the species of candida must be identified due to the inherit resistance of some species to specific antifungal medication classes. Fluconazole 800mg loading dose, then 400mg daily is commonly used in C. albicans infections.[2,3] C. glabrata has developed growing resistance to fluconazole, and cross-resistance to

voriconazole (Vfend), thus echinocandins are first line.[3,5] Examples and doses of echinocandins include anidulafungin (Eraxis) 200mg loading dose then 100mg IV once daily, caspofungin (Cancidas) 70mg loading dose then 50mg IV once daily, or micafungin (Mycamine) 100mg IV once daily. [2,3,5]

Treatment of fungal infections provide pharmacists an additional opportunity to impact the quality of patient care. It is vital to consider the site and species of Candida when evaluating potential treatment options. A positive Candidia cultures does not mean treatment is always warranted (normal microbiome), but suboptimal treatment can increase a patient's length of stay and decrease a patient's quality of life.

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New Drug Update- Andexanet Alfa: Andexxa

By Youssef Bessada, PharmD Candidate, ACPHS Class of 2020

Andexanet alfa (Andexxa™) is a recombinant modified human factor Xa decoy protein manufactured by Portola Pharmaceuticals, approved in May of 2018, that has shown to reverse the inhibition of factor Xa in healthy volunteers. Andexxa™ binds and sequesters the factor Xa inhibitors or Direct Oral Anticoagulants (DOACs) rivaroxaban and apixaban, in addition to inhibiting the activity of Tissue Factor Pathway Inhibitor (TFPI), and increasing tissue factor-initiated thrombin generation.[1] Dosing of Andexxa™ is based on the dose of the DOAC being reversed and time since the patient's last dose. It is available as a lyophilized powder in single-use vials of 100 mg ($3,300.00/vial) or 200 mg ($6,600.00/vial) and administered as an initial IV bolus, with a target of 30 mg/min, followed by continuous infusion for up to 120 minutes. Major warnings for Andexxa™ include arterial and venous thromboembolic events, ischemic events and cardiac events, including sudden death and re-elevation or incomplete reversal of anticoagulant activity. This medication has a rapid onset and pharmacodynamic half-life of ~1 hour, making this a novel therapy for acute bleeding associated with DOAC use. The FDA approved indication of Andexxa™ is for patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.[1, 2]

Phase 1 data for andexanet involved subjects (n = 32) randomized in a 6:2 ratio to single IV bolus doses of placebo or andexanet 30, 90, 300, or 600 mg, with patients followed for 28 days. Both the Cmax (maximum serum concentration) and the AUC of andexanet increased relatively proportionally with increasing doses above 30 mg and no adverse effects were considered serious or attributed to andexanet.[3] The Phase 2 studies of andexanet randomized subjects in a 6:3 ratio to one of six doses of andexanet bolus-only, or andexanet-bolus and infusion, or placebo; for apixaban, rivaroxaban, edoxaban, and enoxaparin, and andexanet was administered 3 hours after the last dose of the factor Xa inhibitor. Subjects receiving the 420 mg bolus dose of andexanet with the 2 hour infusion demonstrated a sustained reduction in unbound apixaban plasma concentrations for 3 hours ($p < 0.05$ vs. pooled cohorts), which returned to placebo levels in 0.17 to 3.5 h. 240 mg and 420 mg bolus doses of andexanet reduced unbound rivaroxaban plasma concentrations by 32% and 51%, respectively, as well as producing a 20% and 53% reduction in anti-Xa activity, respectively. Using 600 mg and 800 mg bolus doses followed by 8mg/min infusions of andexanet for 2 hours, the anti-Xa activity of edoxaban was reduced by 52% and 73%, respectively, compared to baseline. Similarly, anti-Xa activity from enoxaparin was reduced by 67%, and inhibition of thrombin generation was reversed to baseline levels after the andexanet bolus dose.[4]

Once dosing from phase 2 trials had been determined, these doses were evaluated in the Andexanet Alfa, a Novel Antidote to the Anticoagulation Effects of FXA Inhibitors Apixaban (ANNEXA-A) and Rivaroxaban (ANNEXA-R) trials. The ANNEXA –A and ANNEXA-R trials were randomized, double-blind, placebo-controlled studies in which subjects 50–75 years old were enrolled. Subjects were randomized in a 3:1 ratio (ANNEXA-A) or 2:1 ratio (ANNEXA-R) to receive andexanet or placebo. The primary outcome of the trial was the percent change in anti-Xa activity from baseline, 2-5 min after the andexanet bolus (part 1) and at 5-10 min before the end of the infusion (part 2). Subjects in the ANNEXA-A trial received apixaban 5 mg twice daily for 3.5 days (7 doses) to achieve steady state anticoagulation. At 3 hours after the last dose of apixaban (peak concentration), andexanet was given as an IV bolus of 400 mg over about 15 minutes, followed by an infusion of 4 mg/min for 2 h (480 mg total). In the ANNEXA-R trial, subjects received rivaroxaban 20 mg daily for 4 days (4 doses) for steady state anticoagulation. At 4 hours after the last dose (peak concentration), andexanet was given as an IV bolus of 800 mg over about 30 minutes, followed by an infusion of 8 mg/min for 2 hours (960 mg total). In patients receiving apixaban, the anti- Xa activity was reduced by 94% after the bolus of andexanet compared to 21% in those receiving placebo ($p < 0.001$). Similar results were seen in patients receiving rivaroxaban, with a reduction in anti-Xa activity of 92% with the andexanet bolus compared to 18% with placebo ($p < 0.001$). These reductions were maintained throughout the 2-hour infusion and returned to placebo level in 1 to 2 hours after discontinuation of andexanet. Andexanet also produced significant reductions in unbound apixaban and rivaroxaban plasma levels, increased thrombin generation, and significantly more patients achieved an 80% reduction in anti-Xa activity compared to placebo.[5,7]

Prior to the release and approval of Andexxa™, the guideline for reversal of antithrombotics in intracranial hemorrhage by the Neurocritical Care Society and Society of Critical Care Medicine was released in 2015 and reviewed the anticoagulation reversal options in the acute, emergent setting of intracranial hemorrhage. The guidelines described activated charcoal, prothrombin complex concentrates (PCC), activated PCC (aPCC), four-factor PCC and fresh frozen plasma (FFP) as the possible reversal options for DOACs. Guidelines recommended activated charcoal (50 g) be administered to intubated intracranial hemorrhage patients and/or those at low risk of aspiration who present within 2 hours of ingestion of a DOAC. This recommendation was based on a study which found that 50 g of activated charcoal, 2 hours after a single dose of 20 mg of apixaban reduced exposure to the drug by 50% in healthy volunteers. Guidelines also recommended that 4-factor PCC (50 U/kg) or activated PCC (50 U/kg) if intracranial hemorrhage occurred within 3–5 terminal half-lives of drug exposure or in the context of liver failure. This recommendation is based on studies on healthy volunteers that have shown partial or complete reversal of rivaroxaban-induced coagulation abnormalities with 4-factor PCC (50 U/kg), aPCC (25 and 80 U/kg) and rFVIIa. All other anticoagulation reversal options were not recommended, and the recommendations made in 2015 were conditional recommendations with very low- and low-quality evidence, respectively.[6] At the time, this was suggestive of the need of an efficacious therapy and based on the ANNEXA-A/-R trials, set the precedent for significant potential impact of andexanet alfa in the acute, emergent setting of acute bleeds associated with DOACs.

In September of 2019, a pharmacist-led manuscript was formulated to review the pharmacology, preclinical data and clinical data available for the specific antidotes for reversal of DOACs and included the use and role of andexanet alfa in practice. This review found that the reversal of anticoagulant effect was evident in a number of animal, and healthy human subjects. It concluded that in patients with acute major bleeding, the reversal of anticoagulant activity is consistent with prior trials, as well as >80% of patients achieving excellent or good hemostatic efficacy, which would be the goal of an anticoagulant antidote. In clinical practice, andexanet alfa is an effective therapy in the acute, emergent setting for the reversal of apixaban and rivaroxaban, per the dosing regimens approved in the ANNEXA-4 trial. Approval for reversal of other factor Xa inhibitors will require additional data from Phase 3 and 4 trials and this treatment strategy has not been evaluated for reversal of factor Xa inhibitors in patients requiring urgent major surgery. While a future trial of andexanet is being planned for this indication, the need for urgent surgery within 12 hours is currently a contraindication to use.[7]

Based on the results of the ANNEXA-A / R trials and the finding of the role of andexanet alfa in the clinical practice setting, andexanet alfa is a useful and efficacious medication for the treatment of acute and emergent

bleeding associated with DOAC use. The major limitation to its usage on hospital formularies stems from the steep price per vial and can be suggested to be included in emergent situations with no other available options to prevent mortality in acute, critical care patients.

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Sweet Salvation: the FDA Approves Two New Glucagon Formulations for Treatment of Severe Hypoglycemia

By Madyson Allard, PharmD Candidate, ACPHS Class of 2020

Glucose is essential for the body, as it is the body's main source of energy. Very low blood glucose levels, known as severe hypoglycemia, is a medical emergency requiring immediate treatment. For patients with diabetes receiving exogenous insulin therapy, hypoglycemia is a dangerous side effect that can be fatal if untreated. Symptoms of low blood sugar include diaphoresis, shakiness, fatigue, and irritability. Patients with severe hypoglycemia may also present with confusion and abnormal behavior, blurred vision, and loss of consciousness or seizures.[1]

Exogenous glucagon is indicated as an emergent treatment for severe hypoglycemia. Glucagon promotes hepatic glycogenolysis and gluconeogenesis, which raises blood glucose levels.[2] The original commercial formulations of this medication exist as a powder that requires reconstitution prior to use. The prepared medication then has to be injected intramuscularly. Reconstitution and administration of glucagon requires a skill that may prove difficult to caregivers responding to the medical emergency of hypoglycemia.[3] The FDA has recently approved two new formulations of glucagon that can help alleviate these challenges, while providing the same stability and efficacy of this life saving medication.

The first of the two new FDA approved formulations is Baqsimi, a nasal powder formulation approved for patients with diabetes age four and older.[6] This formulation mimics the delivery system of opioid reversal agents in instances of opioid overdose utilizing an intranasal plunger, and allows administration without an injection. This formulation has proven to be easier and faster to administer than the original injectable version. The intranasal formulation has proven to be equally efficacious in raising blood glucose when compared to the intramuscular formulation, producing at least a 25 mg/dL rise if glucose within 20 minutes of dose administration. Administered intranasally, Baqsimi can be used in an unconscious patient because it does not require inhalation. The medication remains effective in instances of a cold or in patients taking cold medicine.[4,6]

The second of the new glucagon formulations is GVOKE; a stable, liquid, ready-to-use injectable. Given the stable liquid formulation, this option also avoids the need for reconstitution. This emergency treatment is stored at room temperature and is approved in patients with diabetes as young as two years of age.[7] This formulation will be available as both a prefilled syringe and an auto-injector. Each formulation will help

alleviate the complicated process of drug reconstitution, reduce concerns of providing a full dose, and, with the auto-injector, may even eliminate the fear of administering an injection. Studies that led to the approval of this formulation demonstrated nearly 100% treatment success rates in administering the full treatment dose. [5,7]

Both new glucagon products have the same contraindications and side effects as the original formulation. Glucagon is contraindicated in patients with pheochromocytoma or insulinoma and common side effects include nausea, vomiting, and hyperglycemia. Allergic reactions have also been reported with use of these agents. [6,7]

As these FDA approvals do not represent a new medication, the safety and efficacy of this emergency agent have already been demonstrated. What these new approvals offer are novel delivery systems to help patients and their caregivers more efficiently treat hypoglycemia. Reducing the complication of reconstitution can reduce error and improve response time to treating patients in a potentially life-threatening situation. With improved treatment for hypoglycemia, patients can feel more comfortable improving their diabetes care with greater confidence in treating a hypoglycemic emergency.

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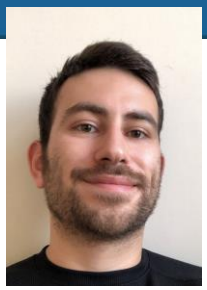
Complications Due to Perioperative Opioid Prescriptions in Children Status-Post Tonsillectomy



By Colin Duell, PharmD Candidate, ACPHS Class of 2022

More than 530,000 tonsillectomies are performed annually in children age 15 years and younger, representing one of the most commonly performed surgical procedures in this population.[1] Addressing the postoperative pain that follows is crucial in order to offer analgesic relief and avoid potential dehydration. Opioids are frequently used to alleviate pain and subsequent discomfort after tonsillectomy even though clinical practice guidelines advise against their use in these cases.[2] It has been widely held that opioids provide optimal analgesic effect compared to non-opioid medications such as non-steroidal anti-inflammatory drugs (NSAIDs). Historically, NSAIDs have also been believed to increase bleeding risk in these patients post-operatively.[1] However, these criticisms of NSAID use have recently been debunked. Randomized clinical trials have found that NSAIDs provide equivalent analgesic effects after a tonsillectomy compared to opioid medications[2], and several studies have concluded that the use of NSAIDs post tonsillectomy does not increase bleeding risk.[2,3]

With the ongoing opioid epidemic, efforts are underway to reduce the use of opioid prescriptions. A recent cohort study, where data were collected through a database of national private insurance claims, compared the risk of complications of perioperative opioid and non-opioid prescriptions after tonsillectomy in children. The analysis consisted of 15,793 children aged 1-18 years old, residing in the USA, and status-post tonsillectomy in

2016 or 2017. The study found there was no difference between opioid and non-opioid groups in the number of return visits for pain, dehydration, or secondary bleeding. However, children having one or more perioperative opioid prescription filled were more likely to have an increased risk of return visits for a medication averse effect (constipation), an increased risk of respiratory complications, and were more likely to experience new and persistent opioid use, compared to children receiving a non-opioid prescription.[4] Results of this study further support the recommendations of the American Academy of Otolaryngology, which recommends non-opioids as a first-line option for post- tonsillectomy analgesia in children.[2]

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Questions?

Please Contact:
Bennett Doughty, PharmD, BCPS, BCPP
NYS-ACCP Secretary/Treasurer
Bennett.Doughty@gmail.com