2020

Dalbavancin in the Community Emergency Department

Wesley Johnson
wesley.johnson@uky.edu

STUDENT AGREEMENT:

I represent that my capstone and abstract are my original work. Proper attribution has been given to all outside sources. I understand that I am solely responsible for obtaining any needed copyright permissions. I have obtained needed written permission statement(s) from the owner(s) of each third-party copyrighted matter to be included in my work, allowing electronic distribution (if such use is not permitted by the fair use doctrine) which will be submitted to UKnowledge as Additional File.

I hereby grant to The University of Kentucky and its agents the irrevocable, non-exclusive, and royalty-free license to archive and make accessible my work in whole or in part in all forms of media, now or hereafter known. I agree that the document mentioned above may be made available immediately for worldwide access unless an embargo applies.

I retain all other ownership rights to the copyright of my work. I also retain the right to use in future works (such as articles or books) all or part of my work. I understand that I am free to register the copyright to my work.

REVIEW, APPROVAL AND ACCEPTANCE

The document mentioned above has been reviewed and accepted by the student's advisor, on behalf of the advisory committee, and by the Director of Graduate Studies (DGS), on behalf of the program; we verify that this is the final, approved version of the student's capstone including all changes required by the advisory committee. The undersigned agree to abide by the statements above.

Wesley Johnson, Student

Julia Costich, Committee Chair

Dr. Sarah Wackerbarth, Director of Graduate Studies

Dalbavancin in the Community Emergency Department

CAPSTONE PROJECT PAPER

A paper submitted in partial fulfillment of the

Requirements for the degree of

Master of Public Health in the

University of Kentucky College of Public Health

By

Wes Johnson

Bowling Green, Kentucky

Final Examination:

Online on April 17, 2020

Capstone Committee:

Julia F. Costich, JD, PhD (Chair)

Kathi Harp, PhD (Co-Chair)

Sarah Cotner, PharmD

Acknowledgments

Thanks to Dr. Cotner for giving me the opportunity to help with this project.
Thanks to Dr. Costich and Dr. Harp for all their help as Chair and Co-chair.
I appreciate each of these individual's time and commitment to helping me achieve my goals. I cannot say thank you enough for all they did to help me.

Abstract

Introduction

Dalbavancin is an antibiotic within the class of medications known as lipoglycopeptides. This medication is given to patients presenting to the hospital with acute skin and skin-structure infections (ABSSSI). This is a unique medication because it is given as a one-time dose in the outpatient setting and it could prevent patients from requiring admission to the hospital.

Methods

The emergency department (ED) at Good Samaritan community hospital performed a trial period with dalbavancin and data was collected from November 2018 to March 2020. Retrospective chart review was performed to obtain patient data and outcomes. Patients would be contacted by a clinical pharmacist within 72 hours of treatment.

Results

Ten patients received dalbavancin in the ED during the trial period. Two patients were reached on follow-up and noted improvement in the initial lesion. Two patients returned to the ED within 30 days, and one of these patients was admitted.

Discussion

Dalbavancin provides another therapy option to the treatment of ABSSSIs. The one-time dosing is advantageous for outpatient treatment of patients presenting with ABSSSIs. This case series suggests dalbavancin can have positive effects when implemented in community hospital settings.

Keywords: Dalbavancin, acute bacterial skin and skin-structure infections, emergency department, outpatient, community hospital

Table of Contents

List of Abbreviations

ABSSSI – Acute bacterial skin and skin-structure infection

BC – Blood Culture

E. Coli – *Escherichia coli*

ED – Emergency department

FDA – Food and Drug Administration

GS – Good Samaritan

HLD - Hyperlipidemia

HTN - Hypertension

H&P – History and Physical

ICU – Intensive care unit

IDSA – Infectious Diseases Society of America

IRB - Institutional Review Board

IV – Intravenous

IVDU – Intravenous drug user

MRSA - Methicillin-resistant *Staphylococcus aureus*

MSSA – Methicillin-susceptible *Staphylococcus aureus*

OPAT – Outpatient parenteral antibiotic therapy

T2DM – Type 2 diabetes mellitus

UK – University of Kentucky

UTI – Urinary tract infection

WBC – White blood cells

Introduction

Acute bacterial skin and skin-structure infections (ABSSSI) is a common reason that patients present to emergency departments (ED) (1). The causative pathogen in patients presenting with ABSSSI is typically gram-positive organisms, particularly *Staphylococcus aureus* (2). Patients have several options for treatment. These options include inpatient or outpatient treatment in combination with intravenous (IV) or oral antibiotics.

With such a range of treatment options it becomes difficult to determine what treatment is best for patients presenting with ABSSSIs. Inpatient treatment is typically reserved for more severe cases of ABSSSIs that may need additional supportive care, and outpatient treatment provides a convenient option for patients that present with milder cases of ABSSSIs. Patients treated in the outpatient setting have successful outcomes and avoid the inconvenience of being admitted to the hospital (3). Outpatient treatment typically consists of oral antibiotics for ABSSSIs. Newer antibiotics have been developed that allow patients to receive treatment in the outpatient setting in order to avoid admission to the hospital for the sole purpose of receiving IV antibiotics. This class of antibiotics is known as lipoglycopeptides and includes dalbavancin (4). Dalbavancin's single IV infusion regimen is Food and Drug Administration (FDA) approved for the indication of ABSSSI that are caused by susceptible organisms (5). Due to the convenience of one-time dosing, patients can avoid hospital admission and receive adequate coverage for the majority of ABSSSI cases.

Dalbavancin has positive public health implications. Namely, it provides another option to the armamentarium of medications used for ABSSSI. Use of dalbavancin also provides convenience for patients and providers through its one-time administration. Dalbavancin also allows patients to receive adequate outpatient treatment and thus avoid a hospitalization for the treatment of ABSSSI.

Dalbavancin is currently used at the ED associated with the University of Kentucky's (UK) academic medical center. UK's academic medical center has many resources such as ED pharmacists and attending physicians, as well as infectious disease pharmacists and physicians. Access to these resources and personnel allow for proper administration, documentation and follow-up for dalbavancin through a collaborative institutional protocol. The community hospital associated with UK, known as Good Samaritan, does not have a dedicated ED pharmacist at this time. A trial period of dalbavancin utilization was initiated at Good Samaritan's ED. The trial period was initiated in November of 2018 and included 10 patients.

This retrospective case series was performed for patients that received dalbavancin within the ED at Good Samaritan Hospital. This case series aims to describe the results of patients receiving dalbavancin at Good Samaritan, as well as identify areas of process improvement for the administration of dalbavancin within a smaller community ED setting.

Literature Review

Presentation of ABSSSI

ABSSSI is a common condition that is seen by practitioners within emergency departments. The FDA defines ABSSSI as cellulitis/erysipelas, wound infection, and major cutaneous abscess, with a surface area of the lesion greater than or equal to $75m^2$. In addition, there are two categories of ABSSSI: purulent, which includes cellulitis and erysipelas, and nonpurulent, which includes abscesses (6). The variation could range from those presenting with minor cases of uncomplicated cellulitis to those presenting with a major cutaneous abscess, along with systemic symptoms (7). While these patients can have a multitude of presentations, initial treatment will typically be directed towards gram-positive cocci (4). Others present with gram-negative pathogens, anaerobes or a mixture. These patients can typically be identified through specific risk factors and comorbidities that are listed in table 1 (8).

Table 1. Gram Negative Organism Risk Factors

Risk Factors for Gram-Negative or anaerobic infections	**Co-morbidities associated with gram-negative or anaerobic infections**
Surgical site infections Axillary cavity Gastrointestinal tract Perineum Female genital tract	Diabetes mellitus Cirrhosis Intravenous drug abuse Subcutaneous drug abuse

Patients that present to the ED with ABSSSI can be treated in the outpatient

setting and the Infectious Diseases Society of America (IDSA) recommends this route of treatment, when possible (9). However, there are patients that present to the ED that will ultimately need to be hospitalized. Determination of proper route of treatment is subjective and can vary between providers. One study found that patients were most likely to be hospitalized when they needed IV antibiotics, had a history of fever, presented with a larger lesion, had any co-morbidity and were age >65 years. However, the study also found that nearly all the patients were admitted to non-critical areas and few had serious complications. This finding raises the possibility that patients could have experienced successful outcomes with outpatient treatment (10). It must also be considered that patients treated within the inpatient setting are exposed to risks such as adverse drug reactions and infection (11).

Treatment of ABSSSI

Patients that present to the ED with ABSSSI have a multitude of treatment options. These treatments are typically aimed at gram-positive organisms such as *Staphylococcus aureus* and *Streptococcus* spp. (12). The 2019 review to the IDSA ABSSSI guidelines notes that methicillin-resistant *Staphylococcus aureus* (MRSA) needs to be considered when treating patients who present with ABSSSI (4). This consideration is paramount within areas that have higher rates of MRSA demonstrated by antibiogram patterns. There are many drugs that have good activity against MRSA, but it becomes difficult to determine which choice is the best for patients presenting to the ED with ABSSSI.

Table 2. Antibiotics Available for ABSSSI Treatment

Drug	Considerations in therapy
Vancomycin	Drug of choice for MRSA; requires drug monitoring; nephrotoxic effects; IV only
Linezolid	Bacteriostatic; hematologic effects; oral or IV
Tedizolid	Bacteriostatic; hematologic effects; oral or IV
Clindamycin	Bacteriostatic; inducible resistance with MRSA; risk of *Clostridioides difficile*; oral or IV
Daptomycin	Bactericidal; potential for myopathies; IV only
Ceftaroline	Bactericidal; IV only
Doxycycline	Bacteriostatic; oral or IV
Trimethoprim-sulfamethoxazole	Bactericidal; oral or IV
Delafloxacin	Tendon rupture; CNS effects; oral or IV
Omadacycline	Oral or IV
Dalbavancin	Bactericidal; IV only; single infusion
Oritavancin	Bactericidal; IV only; single infusion

As noted in table 2, there are many options for treatment of patients presenting with ABSSSI. Vancomycin is the drug that is commonly started as the initial treatment for patients presenting with more severe ABSSSIs. Vancomycin is chosen due to its superb coverage of gram-positive organisms, as well as its effectiveness against MRSA (13). However, vancomycin is an IV drug that is typically given twice daily, and patients will often be admitted to the hospital in order to receive the proper dosing.

Drawbacks to the use of vancomycin include risk of kidney injury with high trough concentrations (>20mg/L), higher daily doses (>4g per day), longer duration of therapy (>7 days) and concomitant dosing with other antimicrobials such as piperacillin-

tazobactam (14, 15). Due to the risk of nephrotoxicity, vancomycin requires therapeutic drug monitoring and dosage adjustments that can be time and labor intensive (16).

Conversely, patients that present to the ED with ABSSSI and mild to no systemic symptoms can be candidates for outpatient treatment. Outpatient is preferred, when possible, due to cost savings and the avoidance of unintended consequences associated with hospital admissions (3, 11). Traditionally, patients that receive outpatient treatment will receive oral medications due to the convenience from a patient's perspective. As noted in table 2, there are several medications that have oral options, which include linezolid, doxycycline and trimethoprim-sulfamethoxazole. These all have coverage against MRSA and can be effective options when a patient is deemed to be a candidate for outpatient therapy. In addition, patients that are admitted to the hospital to receive IV antibiotics may be discharged within a few days after showing signs of improvement and then can be switched to oral antibiotics to finish a 7 to 10-day treatment course (4).

Patients can receive IV antibiotics within the outpatient setting and this is known as outpatient parenteral antibiotic therapy (OPAT). The IV medications will be administered through a temporary IV line that is placed. This method allows patients to receive proper antibiotic therapy within their own home, an infusion center or a long-term medical facility. This method is a convenient option for patients that have help from caregivers or in-home medical staff (home health nurses, etc.). However, not every patient is a candidate to receive OPAT. There needs to a competent and adherent patient or caregiver within the home of a patient receiving OPAT. This adult also must be able to

learn and perform sterile infusion, as well as communicate with a medical team (17). Any of the IV drugs listed in table 2 can be utilized for patients within the outpatient setting.

There are several downsides to utilizing OPAT. As mentioned, this option requires patients to have an IV access line placed and this can lead to adverse events. This IV access line can become infected without proper sanitizing techniques, or a clot can develop, which prevents drug from being properly administered through the line. In addition to this, several antibiotics need therapeutic drug monitoring due to risk of incorrect drug concentration levels and this requires weekly check-ups with a healthcare provider (17).

Dalbavancin is a new IV medication that can be used within the outpatient setting. It is unique in the fact that it is a single IV dose which is FDA-approved for the treatment of ABSSSIs. The convenience of a one-time dose is very appealing to patients, and it avoids therapeutic drug monitoring or the need for an IV access line to be placed. Also, proper dalbavancin utilization could lead to cost savings through avoidance of inpatient hospital days (18). Dalbavancin has a favorable side effect profile with mild adverse reactions being identified. The major adverse events include nausea, headache and diarrhea. Also, dalbavancin has little effect on cytochrome P450 substrates and therefore there are few clinically relevant drug interactions (5).

<u>Outpatient dalbavancin versus inpatient treatment</u>

The FDA's approval of dalbavancin for the treatment of ABSSSI raises the question

of dalbavancin's place in therapy. Studies note that one role in therapy could be for patients that are being admitted to the hospital for the sole purpose of receiving IV antibiotics. Talan et al found that 41.5% of patients presenting with ABSSSI were admitted to the hospital for the sole purpose of receiving IV antibiotics and none of these patients required intensive critical unit (ICU) transfer (10). This finding demonstrates that many patients could utilize outpatient therapy due to the lack of high-level care needed. To add to this, data from 2008 to 2010 showed that patients presenting with ABSSSIs that were subsequently hospitalized, had a mortality of 0.5%. This statistic demonstrates that many ABSSSI patients have no need to be hospitalized (19). Assuming these patients have no contraindications to dalbavancin, this could be the area where dalbavancin could be utilized for cost-savings and patient convenience.

Another study compared the use of vancomycin followed by oral linezolid to the use of dalbavancin weekly for the treatment of patients with ABSSSIs. Specifically, these were patients with one or more systemic signs of infection who were thought to need at least three days of IV therapy (20). Previously dalbavancin had been approved for a regimen of 1 gram on day 1 followed by 500mg on day 8, but it was later proved that a single 1500mg infusion was noninferior (21). The study found that dalbavancin was not inferior to the conventional regimen of IV plus oral antibiotics. In addition to this, patients receiving dalbavancin had fewer side effects as compared to those that received vancomycin-linezolid combination (20).

There is good evidence for using dalbavancin for patients that would typically be

admitted to the hospital for the sole purpose of receiving IV antibiotics. However, it becomes important to understand when patients are not candidates for dalbavancin and should be admitted to the hospital. Currently there is not a definitive algorithm for when patients should be hospitalized due to an ABSSSI. IDSA guidelines note that patients that should likely be admitted to the hospital include those with signs of sepsis, suspicion of deep tissue infections (i.e. necrotizing fasciitis), or exacerbation of comorbidities (4). These patients are best managed within the inpatient setting due to medical concerns that go beyond a skin infection. Also, if a patient presents with symptoms or comorbidities listed in table 1, they will need additional coverage that typically warrants admission to the hospital.

Use of dalbavancin at the University of Kentucky Medical Center

Currently, dalbavancin is utilized within the University of Kentucky emergency department and has shown favorable outcomes. In 2016, a case series was performed in order to assess the feasibility of using dalbavancin (22). The antimicrobial stewardship team at UK developed guidelines to allow for proper selection of patients who could receive dalbavancin. As the literature shows, the guideline first determined whether the patient would be admitted to the hospital for IV antibiotics to treat ABSSSI. If the patient is 18 years of age or older and has a lesion 75 cm^2 or greater, then they become a candidate for dalbavancin. However, there are several contraindications to the use of dalbavancin, which are listed in table 3 (23).

Table 3. Contraindications to Dalbavancin

Contraindications to dalbavancin
- Diabetic foot infection/compromised vascularity - Necrotizing fasciitis/gangrene - Altered mental status - Prior antibiotic failure and requires inpatient support - Bacteremia, endocarditis, osteomyelitis, catheter infection - Unstable comorbidities (ex: diabetic ketoacidosis, acute exacerbation) - Immunocompromised (ex: CD4 < 200 cells/mm3 , neutrophils < 500 cells/mm3 , uncontrolled diabetes) - Burn - Severe sepsis/shock - Severe vancomycin allergy - Severe hepatic disease - Surgical site infection - Pregnancy

Following up with patients that receive dalbavancin is an important part of the treatment algorithm. The protocol developed at UK has the emergency department pharmacist follow-up with patients within the next 72 hours to monitor improvement. This is the time period when most patients experience clinical improvement and is an endpoint that has been used for outcomes in previous studies (24). After the follow-up interaction, patient's clinical outcomes are recorded within REDCap™ (22).

The University of Kentucky has a community hospital that is affiliated with their healthcare system, Good Samaritan Hospital. This community hospital is a smaller institution that is equipped with an ED. However, Good Samaritan's ED does not have an emergency department pharmacist on site, who is typically responsible for screening, documentation and follow-up, as it relates to dalbavancin. Thus, dalbavancin is utilized

less frequently at Good Samaritan's ED and it remains to be seen if dalbavancin will be effective within this community hospital.

Purpose

This case series was performed to describe the results of utilizing dalbavancin within the community hospital setting at Good Samaritan's ED. The primary goal of this case series was to assess patient outcomes for those that received dalbavancin within Good Samaritan's ED from November 2018 to March 2020. The secondary goal was to determine process improvement areas, including follow-up and documentation opportunities.

Methods

All data were extracted from electronic medical records (EMR) of patients that presented to the ED at Good Samaritan Hospital. Approval was obtained from the University of Kentucky Institutional Review Board (IRB) to extract and analyze retrospective health record data for patients that received dalbavancin within the ED at Good Samaritan Hospital. The approved time period for data collection begins in November, 2018, and ends October 26, 2020. The inclusion criteria for the case series were patients ≥18 years of age with an ABSSSI ≥ 75 cm^2 that had received dalbavancin at Good Samaritan's ED from November 2018 to March 2020. The business partner director for pharmacy services at UK was able to obtain the correct patient records based on billing for dalbavancin. Patients were also identified by performing a keyword search in the admission History and Physical (H&P).

Through retrospective chart review, the patient characteristics were determined. Patients' age and gender were pulled directly from the patient profile. The ED admission note was reviewed for the determination of each patient's diagnosis, comorbid conditions and any past medical history related to ABSSSIs, as well as any hospital visits after the administration of dalbavancin.

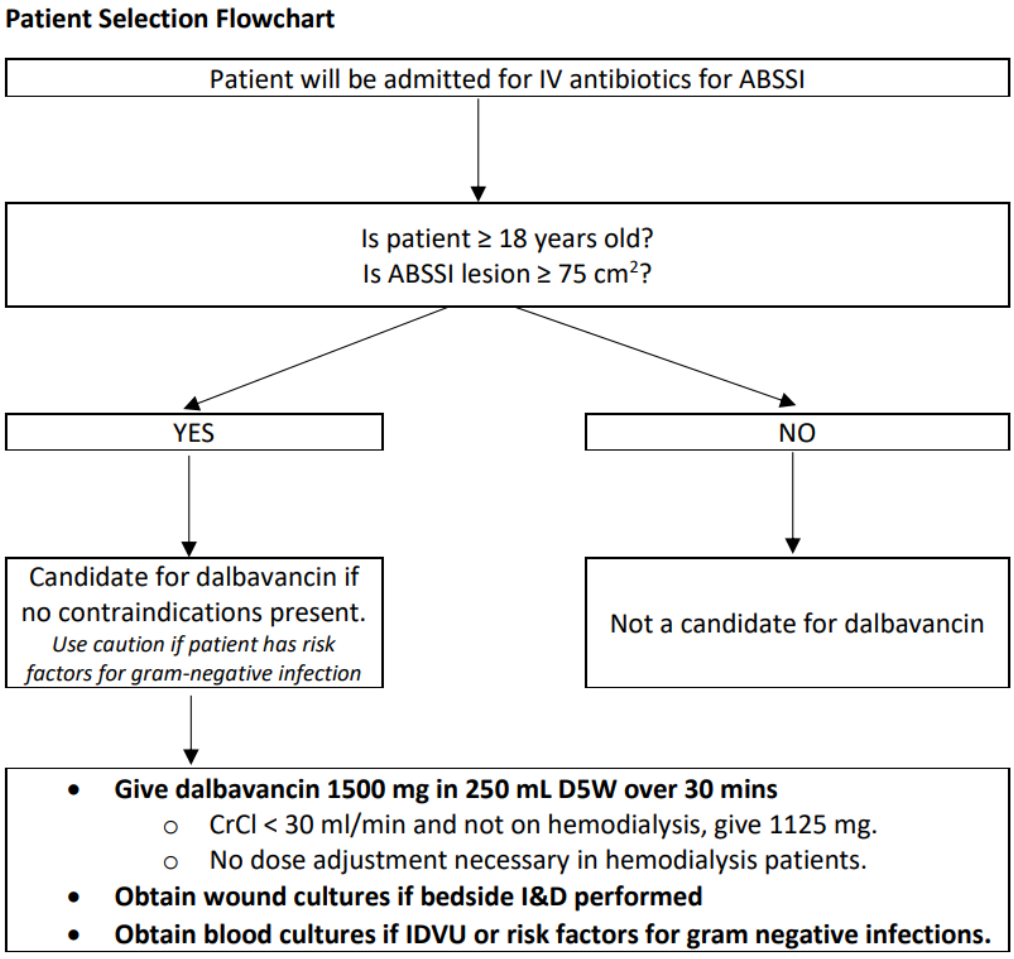
Because dalbavancin administration was a new process, physicians needed to ensure patients were appropriate candidates for dalbavancin therapy. Table 4 (23) identifies those who would need to be contacted for approval of dalbavancin administration. There was documentation within each patient's profile to describe the

appropriateness of dalbavancin. All other information related to the screening process, additional therapy, administration of dalbavancin and the patient follow-up were located in this documentation. The dalbavancin screening determination process is presented in figure 1 (23).

Table 4. Provider Approval for Dalbavancin Administration

Day	Time	Provider Approval Needed
Weekdays	0600 - 1800	ED Attending Physician GS Clinical Pharmacist On Call ID Pharmacist or Physician
	1800 - 0600	ED Attending Physician GS Operations Pharmacist
Weekends	0600 - 1800	ED Attending Physician GS Clinical Pharmacist On Call
	1800 - 0600	ED Attending Physician GS Operations Pharmacist

Figure 1. Dalbavancin Approval Algorithm



Results

From November 2018 to March 2020, patients that received dalbavancin were identified. At the end of the trial period, ten patients had received dalbavancin. The average age of patients receiving dalbavancin was 42.7 years, with a range of 23 to 68. Seven of the patients were female and three male.

During the trial period, the patients' lesions were identified and described. Five (50%) of the patients presenting to the ED had an ABSSSI occurring on their lower extremities. Four (40%) patients presented with ABSSSI occurring on their upper extremities and 1 (10%) presented with ABSSSI on their abdomen.

Most patients during this trial period had documented comorbidities. The most common comorbidity observed in this case series was IV drug use (40%). Other documented comorbidities included hypertension (HTN) (20%), hyperlipidemia (HLD) (20%) and morbid obesity (20%). Wound culture data was obtained for 2 (20%) patients. Dalbavancin properly covered the MRSA found in one patient and the MSSA in the other. The patient with MSSA also had growth of *Escherichia coli* and *Enterobacter cloacae*, this patient received an additional antibiotic due to the gram-negative organisms.

Two patients were contacted for follow-up within 72 hours, one of which received an incision and drainage of abscess the next day. A third patient returned to the ED within 72 hours, and a fourth patient returned 16 days later to be admitted due to a gram-negative organism, *Pseudomonas fluorescens*, in the bloodstream. The two patients

contacted noted improvement in their initial lesion. The third patient that returned to the ED within 72 hours presented with new skin lesions. This patient noted improvement in their initial lesion, but due to an underlying condition this patient presented with new skin lesions. The patient that was admitted 16 days later for *Pseudomonas fluorescens* in their bloodstream also had a positive wound culture showing MRSA. This patient received oral levofloxacin for their bacteremia.

Adverse effects were minimal, as they were only noted in two (20%) patients. One patient experienced nausea during their infusion of dalbavancin. The other patient experienced dizziness during their infusion of dalbavancin.

Table 5. Results of Dalbavancin administration

Gender	Age	ED Diagnosis	Comments/Notes	Comorbid Conditions	I&D	Outcome
F	59	Cellulitis of right lower extremity	Previous use of antibiotics for cellulitis with Bactrim and Keflex, no cultures taken, WBC of 6.94, dizziness experienced during infusion	HTN, morbid obesity, T2DM, HLD	N/A	Follow-up phone call from ED pharmacist - patient reported improvement
F	68	Cellulitis of right upper extremity	Had previous episodes of cellulitis and had taken clindamycin, negative BC, WBC of 14	Breast cancer	N/A	No follow-up information
M	38	Cellulitis of right upper extremity	Frequent hospital visits due to IV drug abuse, negative BC, WBC of 6.8	IVDU	N/A	No follow-up information, subsequent hospitalizations due to IVDU
F	37	Cellulitis of bilateral lower extremities	Negative BC, WBC of 13.8	IVDU	N/A	No follow-up information
F	28	Stomach abscess	Patient was on chronic doxycycline and had recently been taking clindamycin as well for abscesses, negative BC, WBC of 14, nausea experienced during infusion	Hidradenitis suppurativa, morbid obesity, asthma	N/A	Patient returned to ED with new abscess but noted improvement on the initial abscess
F	28	Abscess of right arm	History of failed oral antibiotics, signs of UTI, positive BC for *Pseudomonas fluorescens*, WBC of 7.3	IVDU, endometriosis, HPV	Yes - MRSA	No follow-up, patient presented 16 days later with fever – prescribed levofloxacin due to initial positive BC
F	44	Cellulitis of bilateral upper extremities	Chief complaint was stomach pain, cellulitis was related to injection sites, no BC, WBC of 14.6	IVDU, hepatitis C	N/A	No follow-up information
F	45	Cellulitis of bilateral thighs and buttocks	Received concomitant antibiotics for STD prophylaxis and UTI, negative BC, WBC of 7.2	Chronic back pain	N/A	No follow-up information
M	57	Cellulitis/abscess of right lower extremity	Presented to ED next day due to positive BC for *Staphylococcus aureus*, received abscess I&D, WBC of 16.2	HTN, HLD	Yes- MSSA, E. coli, *Enterobacter cloacae*	Follow-up phone call from ED pharmacist – patient reported improvement – patient followed up with PCP for other bacteria and received ciprofloxacin
M	23	Bilateral lower extremity cellulitis	Previously hospitalized for cellulitis and received vancomycin with oral transition to Bactrim, negative BC, WBC of 13.4	None	N/A	No follow-up information

Limitations

There are several limitations to this study. This was a retrospective case series with a small sample of 10 patients. All data was extracted from an EMR. In addition, this case series was performed at a single hospital's ED, limiting our ability to draw conclusions. Follow-up information was missing for the majority of patients in this case series. Long-term effects of dalbavancin cannot be properly tracked if follow-up information is not obtained from patients.

Discussion

The case series performed at Good Samaritan's ED showed improvement of symptoms and minimal side effects for those that received dalbavancin for patients who were able to be contacted. This finding suggests that dalbavancin, when implemented properly, may be a viable option for patients presenting to a community ED with an ABSSSI. For the two patients that were contacted within 72 hours, both patients noted improvement of the initial lesion. A third patient returned to the ED for new skin lesions but noted the initial lesion had improved. This patient-reported improvement suggests positive outcomes for those that received dalbavancin and were available for follow-up. This finding aligns with previous studies that show positive outcomes for those receiving dalbavancin for ABSSSIs (20, 25).

Patients with documented follow-up showed improvement but this case series

demonstrates the problem of loss to follow-up. The majority (60%) of patients had no documented follow-up from either the pharmacist or subsequent hospital visits. This is problematic for several reasons. Drug effects cannot be monitored when outcomes are unavailable. It becomes difficult to properly monitor effects of a drug when outcomes cannot be tracked. However, this case study is not alone in experiencing difficulties with patient follow-up. A previous study analyzing the implementation of dalbavancin demonstrated difficulties in following up with patients after they have left the hospital (26).

IV drug abuse was a common comorbidity among patients within this case series. Previous studies have shown that those who inject IV drugs have a greater risk for infectious diseases, including bacterial skin infections (27, 28). The single IVDU in the case series who had culture results showed MRSA as the offending agent. Not only is dalbavancin effective for more difficult pathogens such as MRSA, but it also provides a convenient treatment regimen that can improve compliance. Other outpatient treatments require oral or IV administration over several days, which introduces the risk of patient non-compliance. Dalbavancin is monitored for the one-time dose and eliminates any risk of non-compliance, which is a concern within the IVDU population (29). When a full dose of antibiotics is taken appropriately there is a better chance of successful treatment and a lower chance of antibiotic resistance.

Non-compliance is not a problem that is specific to IVDU. Previous studies have shown that the population in general has poor adherence rates, with nearly 15% stopping

their antibiotics early (30). Noncompliance puts patients at risk of treatment failure in the short term. In the long term, non-compliance contributes to the public health issue of antibiotic resistance. This problem may not present as quickly as treatment failure, but antibiotic resistance still has far-reaching effects. Infections with antibiotic resistant organisms are harder to treat and can have worse outcomes. The CDC estimates that nearly 3 million people annually in the U.S. are infected with an antibiotic resistant bacteria or fungi. In addition, the CDC estimates that nearly 35,000 people will die of these difficult-to-treat infections (31). Completing antibiotic courses is a simple yet effective method to combat antibiotic resistance. The one-time dosing of dalbavancin offers an effective solution when providers are concerned about a patient's adherence.

Adverse effects appear to have been minimal in this case series with only two patients experiencing problems associated with dalbavancin administration, although the majority of patients were lost to follow-up. One patient experienced nausea as the infusion was being given. The other patient experienced dizziness that was associated with the infusion. Both reactions align with adverse effects reported in previous dalbavancin studies. The phase III trials that proved the non-inferiority of dalbavancin to comparators showed a favorable side effect profile. These studies noted common side effects to be nausea, diarrhea, and pruritus (20). These are mild side effects when compared to the side effects of similar drugs such as vancomycin and linezolid. Vancomycin can be associated with more severe side effects such as acute kidney injury (14). In addition, a serious side effect associated with linezolid is hematologic changes such as thrombocytopenia and anemia (32). If patients were to have a kidney deficiencies

or previous hematologic abnormalities, dalbavancin could be a reasonable alternative as opposed to vancomycin or linezolid.

A potential benefit of dalbavancin is the cost effectiveness. A cost analysis was not performed in this case series, but previous literature shows potential cost-savings from the use of dalbavancin. This is because dalbavancin is traditionally used for patients that would be admitted to the hospital. Instead of incurring the high cost of a hospital stay, patients receive their dalbavancin infusion in the ED and then are discharged. A retrospective study at UK's academic medical center compared the cost of dalbavancin to a group of patients that were admitted to the hospital for ABSSSIs. The patients that received dalbavancin had a direct cost avoidance of $4,560 (33), demonstrating substantial cost-savings when dalbavancin is properly utilized.

Implications

Dalbavancin is a drug that has several benefits when treating ABSSSI. Dalbavancin plays a unique role because it is an outpatient treatment that can be used for patients who would have previously been admitted to the hospital for IV antibiotics. On a larger scale, this case series adds to the growing body of literature that illustrates the potential effectiveness of dalbavancin.

This case series has public health implications regarding antibiotic resistance. More frequent use of dalbavancin has the potential reduce patients' prescription antibiotic nonadherence in patients and thus reduce antibiotic resistance. Healthcare

providers can confirm that patients receive a full antibiotic regimen with the administration of dalbavancin thus ensuring that patients are adequately treated, while mitigating the chance of antibiotic resistance.

At the institutional level, this case series adds to the literature by addressing the outcomes of implementing dalbavancin within a community ED. Community EDs do not have the resources of larger academic medical centers, and this could make it more difficult to justify implementing a new antibacterial such as dalbavancin. This case series provides one example of the processes that could be implemented to begin using dalbavancin. Also, this case series provides insight into the problems that can be encountered when implementing dalbavancin within a community ED.

This case series also demonstrates the infrequent use of dalbavancin. This case series extended over sixteen months but there were only ten patients that received dalbavancin. Providers' comfort with prescribing dalbavancin appears to be an obstacle. Providers know what to expect when prescribing a drug such as vancomycin for ABSSSIs. Dalbavancin, however, is a new drug that has an unconventional dosing regimen. This situation presents an opportunity for pharmacists to educate providers on dalbavancin's place in therapy. In addition, pharmacy staff can work with providers to ensure proper protocols for dalbavancin administration. With these measures in place, cost savings and convenient dosing of dalbavancin can be fully realized (34).

References

1. Rui P, Kang K, Albert M. National Hospital Ambulatory Medical Care Survey: 2013 Emergency Department Summary Tables. Retrieved from: http://bit.ly/2yhLgoG
2. Summanen, P. H., Talan, D. A., Strong, C., McTeague, M., Bennion, R., Thompson Jr, J. E., ... & Finegold, S. M. (1995). Bacteriology of skin and soft-tissue infections: comparison of infections in intravenous drug users and individuals with no history of intravenous drug use. *Clinical infectious diseases*, *20*(Supplement_2), S279-S282.
3. LaPensee, K., & Fan, W. (2012, June). Economic burden of hospitalization with antibiotic treatment for ABSSSI in the US: an analysis of the Premier Hospital Database. In *17th Annual international meeting of the international society for pharmacoeconomics and outcomes research (ISPOR), Washington DC* (Vol. 2).
4. Golan, Y. (2019). Current treatment options for acute skin and skin-structure infections. *Clinical Infectious Diseases*, *68*(Supplement_3), S206-S212.
5. Dalvance® (dalbavancin) for injection [package insert]. Irvine, CA: Allergan, 2016.
6. US Food and Drug Administration. (2013). Guidance for industry. Acute bacterial skin and skin structure infections: developing drugs for treatment. *Food and Drug Administration, Silver Spring, MD. http://www. fda. gov/downloads/Drugs/./Guidances/ucm071185. pdf*.
7. Abrahamian, F. M., Talan, D. A., & Moran, G. J. (2008). Management of skin and soft-tissue infections in the emergency department. *Infectious disease clinics of North America*, *22*(1), 89-116.

8. Russo, A., Concia, E., Cristini, F., De Rosa, F. G., Esposito, S., Menichetti, F., ... & Viscoli, C. (2016). Current and future trends in antibiotic therapy of acute bacterial skin and skin-structure infections. *Clinical Microbiology and Infection*, *22*, S27-S36.
9. Stevens, D. L., Bisno, A. L., Chambers, H. F., Dellinger, E. P., Goldstein, E. J., Gorbach, S. L., ... & Wade, J. C. (2014). Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clinical infectious diseases*, *59*(2), e10-e52.
10. Talan, D. A., Salhi, B. A., Moran, G. J., Mower, W. R., Hsieh, Y. H., Krishnadasan, A., & Rothman, R. E. (2015). Factors associated with decision to hospitalize emergency department patients with skin and soft tissue infection. *Western Journal of Emergency Medicine*, *16*(1), 89.
11. Hauck, K., & Zhao, X. (2011). How Dangerous is a Day in Hospital?: A Model of Adverse Events and Length of Stay for Medical Inpatients. *Medical Care, 49*(12), 1068-1075.
12. Almarzoky Abuhussain, S. S., Burak, M. A., Adams, D. K., Kohman, K. N., Tart, S. B., Hobbs, A. L., ... & Kuti, J. L. (2018, October). Variability in emergency medicine provider decisions on hospital admission and antibiotic treatment in a survey study for acute bacterial skin and skin structure infections: opportunities for antimicrobial stewardship education. In *Open Forum Infectious Diseases* (Vol. 5, No. 10, p. ofy206). US: Oxford University Press.
13. Vancomycin for injection [package insert]. Rockford, IL: Mylan, 2018.

14. Bamgbola, O. (2016). Review of vancomycin-induced renal toxicity: an update. *Therapeutic advances in endocrinology and metabolism*, *7*(3), 136-147.

15. Rutter, W. C., Cox, J. N., Martin, C. A., Burgess, D. R., & Burgess, D. S. (2017). Erratum for Rutter et al., Nephrotoxicity during vancomycin therapy in combination with piperacillin-tazobactam or cefepime. *Antimicrobial agents and chemotherapy*, *61*(4).

16. Darko, W., Medicis, J. J., Smith, A., Guharoy, R., & Lehmann, D. F. (2003). Mississippi mud no more: cost-effectiveness of pharmacokinetic dosage adjustment of vancomycin to prevent nephrotoxicity. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *23*(5), 643-650.

17. Norris, A. H., Shrestha, N. K., Allison, G. M., Keller, S. C., Bhavan, K. P., Zurlo, J. J., ... & Arrieta, A. (2019). 2018 Infectious Diseases Society of America clinical practice guideline for the management of outpatient parenteral antimicrobial therapy. *Clinical Infectious Diseases*, *68*(1), e1-e35.

18. Nair, T., Fitzgerald, J., Ly, B., & Wallace, M. R. (2018). Dalbavancin as a cost effective antibiotic. *Infectious Diseases*, *50*(1), 75–76. https://doi-org.ezproxy.uky.edu/10.1080/23744235.2017.1365169

19. Khachatryan, A., Patel, D., Stephens, J., Johnson, K., Patel, A., & Talan, D. (2014). Skin and Skin Structure Infections in the Emergency Department: Who Gets Admitted?: 115. *Academic Emergency Medicine*, *21*.

20. Boucher, H. W., Wilcox, M., Talbot, G. H., Puttagunta, S., Das, A. F., & Dunne, M. W. (2014). Once-weekly dalbavancin versus daily conventional therapy for skin infection. *New England Journal of Medicine*, *370*(23), 2169-2179.

21. Dunne, M. W., Puttagunta, S., Giordano, P., Krievins, D., Zelasky, M., & Baldassarre, J. (2016). A randomized clinical trial of single-dose versus weekly dalbavancin for treatment of acute bacterial skin and skin structure infection. *Clinical Infectious Diseases*, *62*(5), 545-551.

22. Burgess, D. R., Baum, R. A., Bailey, A., Myint, T., & Wallace, K. L. (2017, October). Impact of an Antimicrobial Stewardship and Emergency Department Initiated Dalbavancin Guideline for Patients with Acute Bacterial Skin and Soft-Tissue Infections. In Open Forum Infectious Diseases (Vol. 4, No. Suppl 1, pp. S267-S267).

23. Burgess, D., Wallace, K., Bailey, A., Baum, R., Myint, T., Cotner, S. (2019). Dalbavancin Protocol for Treatment of Adult Skin and Soft Tissue Infections (SSTI). Unpublished internal document, Antimicrobial Subcommittee.

24. Toerner, J. G., Burke, L., Komo, S., & Papadopoulos, E. (2012). A collaborative model for endpoint development for acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia.

25. Leuthner, K. D., Buechler, K. A., Kogan, D., Saguros, A., & Lee, H. S. (2016). Clinical efficacy of dalbavancin for the treatment of acute bacterial skin and skin structure infections (ABSSSI). *Therapeutics and clinical risk management*, *12*, 931.

26. Heil, E., Martinelli, A., Oliver, W., & Claeys, K. (2018, November). 2362. Emergency Department Resource Utilization After Implementation of a Dalbavancin Pathway

for Skin and Soft-Tissue Infections. In *Open Forum Infectious Diseases* (Vol. 5, No. Suppl 1, p. S703). Oxford University Press.

27. Bassetti, S., Hoffmann, M., Bucher, H. C., Fluckiger, U., & Battegay, M. (2002). Infections requiring hospitalization of injection drug users who participated in an injection opiate maintenance program. *Clinical infectious diseases*, *34*(5), 711-713.
28. Binswanger, I. A., Kral, A. H., Bluthenthal, R. N., Rybold, D. J., & Edlin, B. R. (2000). High prevalence of abscesses and cellulitis among community-recruited injection drug users in San Francisco. *Clinical infectious diseases*, *30*(3), 579-581.
29. Gonzalez, P. L., Rappo, U., Akinapelli, K., McGregor, J. S., Puttagunta, S., & Dunne, M. W. (2018). Treatment of acute bacterial skin and skin structure infection with single-dose dalbavancin in persons who inject drugs. *Drugs in context*, *7*.
30. Grosso, G., Marventano, S., Ferranti, R., & Mistretta, A. (2012). Pattern of antibiotic use in the community: von-adherence and self-prescription rates in an Italian urban population. *Molecular medicine reports*, *5*(5), 1305-1310.
31. Centers for Disease Control and Prevention. (2020, February 10). About Antibiotic Resistance. Retrieved from https://www.cdc.gov/drugresistance/about.html.
32. Gerson, S. L., Kaplan, S. L., Bruss, J. B., Le, V., Arellano, F. M., Hafkin, B., & Kuter, D. J. (2002). Hematologic effects of linezolid: summary of clinical experience. *Antimicrobial agents and chemotherapy*, *46*(8), 2723–2726. https://doi.org/10.1128/aac.46.8.2723-2726.2002

33. Burgess, D. R., Hile, G., Reynolds, J., Cotner, S., Baum, R., Bailey, A. M., ... & Wallace, K. L. (2018, November). 1878. Expanding Kentucky's "One and Done" Tradition: Lipoglycopeptide Administration in the Emergency Department at a Tertiary, Academic Medical Center. In *Open Forum Infectious Diseases* (Vol. 5, No. Suppl 1, p. S537). Oxford University Press.

34. Terriff C. (2017). Transition of Care with Dalbavancin: a Successful Cost-Saving Stewardship Program through Decreased Length of Stay. *Open Forum Infectious Diseases*, *4*(Suppl 1), S491. https://doi.org/10.1093/ofid/ofx163.1265.

Biographical Sketch

Wes Johnson is currently completing his Doctor of Pharmacy and Master of Public Health at the University of Kentucky and will be set to graduate in May of 2020. The area of focus for his Master of Public Health is Health Systems and Policy Analytics Concentration. After graduation he will go on to work as a pharmacy resident at the University of Kentucky Chandler Medical Center.