



Accepted Abstracts

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E: Encore

OR: Original Research

FRS: Fellow/Resident/Student

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1 OR FRS

In Vitro Activity of Colistin alone and in Combination with Meropenem and Tigecycline against 31 Colistin-resistant *Acinetobacter baumannii* strains

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Background

Acinetobacter baumannii resistance to the carbapenems continues to increase in prevalence making reliance on colistin (COL) as a last resort more common. However, an increase in COL-resistant (COL-R) strains has also been recently reported worldwide. The use of COL in combination with other Gram-negative antimicrobials, including meropenem (MEM) and tigecycline (TGC), has been shown to be effective in eradicating MDR *A. baumannii* infections. However, there is little evidence on the in vitro activity of COL in combination with MEM or TGC in MDR *A. baumannii* strains that are further characterized by the COL-R phenotype. The objective of this study was to evaluate the efficacy of COL alone and in combination with MEM or TGC against COL-R *A. baumannii* strains.

Methods

Susceptibility testing via the broth micro-dilution method was conducted on 31 MDR, including carbapenem-resistant and COL-R, *A. baumannii* strains. Single drug minimum inhibitory concentration (MIC) testing as well as the combination MIC testing of COL+MEM and COL+TGC were conducted on each strain. Each strain was evaluated via time-kill analysis (TKA) to assess the synergistic capabilities of each combination therapy. Synergy was defined as a ≥ 2 -log₁₀CFU/ml reduction from the most active single agent, while bactericidal activity was defined as > 3 -log₁₀ CFU/ml reduction from the initial inoculum.

Results

All of the strains were resistant to COL and MEM, demonstrated by an MIC of ≥ 4 mg/l and ≥ 8 mg/l for each antimicrobial, respectively. Elevated MICs of ≥ 4 mg/l were observed for TGC in all strains. In combination MIC testing, COL MICs were reduced up to 512-fold and 32-fold, in the presence of sub-inhibitory MEM or TGC, respectively. MEM and TGC MICs were decreased up to 128-fold and 16-fold in the presence of sub-inhibitory COL, respectively. Utilizing the combination MIC testing, the COL+MEM combination demonstrated synergy in 29/31 (94%) of the strains, while the COL+TGC combination reflected synergy in 18/31 (60%) of the strains.

Conclusions

The combinations of COL+MEM and COL+TGC demonstrate possible therapeutic options in eradicating MDR, including COL-R, *A. baumannii* infections. Further research is warranted to assess the role of the combinations in therapy.

2 OR FRS

Early Experience with Eravacycline for Complicated Infections

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Background

Eravacycline (ERV) received Food and Drug Administration (FDA) approval for the treatment of adults with complicated intra-abdominal infections (cIAIs) in 2018. ERV is a novel fluorocycline with broad-spectrum activity against Gram-positive, Gram-negative and anaerobic bacteria including those with tetracycline-acquired resistance mechanisms. Real-world data regarding ERV use in FDA and non-FDA approved indications is limited. We evaluated the clinical and safety outcomes of patients treated with ERV for various infections.

Methods

Multi-center, retrospective, observational study from December 2018 to October 2019. Adult patients treated with ERV for \geq 72 hours were included. Primary outcome was 30-day survival. Secondary outcomes were 30-day lack of infection-recurrence and resolution of signs/symptoms of infection.

Results

Overall, 35 patients were included from 5 geographically distinct medical centers across the United States. Median(IQR) age was 56 years (48-68) and 63% were male. Median(IQR) APACHE II and Charlson Comorbidity scores were 16 (11-21) and 3 (2-7), respectively. Common sources of infection were intra-abdominal (34%), respiratory (29%), and bone/joint (14%). The most common pathogens were *Klebsiella pneumoniae* (16%), and *Enterococcus faecium* (14%), followed by *Escherichia coli* (12%). Infectious diseases consultation was obtained in (97%), and surgical interventions in (54%). Most patients received active therapy prior to ERV initiation (66%). Median ERV therapy duration was 9(4-18) days. Among cases with documented cultures, ERV was initiated within a median of 7(4-17) days. Combination therapy \geq 48 hours was given in (51%). Thirty-day survival was achieved in 74%(26/35). Of patients who died, majority had positive blood cultures (4/7), intra-abdominal as a source (4/7), were critically ill (4/7), and on monotherapy (4/7). For secondary outcomes; 91% (32/35) lacked 30-day infection-recurrence and 57%(20/35) resolved signs/symptoms of infection. The most common reason to select ERV were consolidation of the regimen (43%). There were 7 probable ERV-related adverse events, most commonly (57%) gastrointestinal and (14%)rash, but only one led to drug discontinuation.

Conclusions

30-day survival was achieved in majority of patients treated with ERV for various infections. Studies with longer follow-up and more patients are required to assess the effectiveness and safety of ERV, particularly compared to standard of care.

Delafloxacin (DLX) in the treatment of Community Acquired Bacterial Pneumonia (CABP): Patients with PORT Risk Class III-V

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Background

DLX is an IV/oral anionic fluoroquinolone approved for treatment of serious skin infections. A global Phase 3 trial of 859 patients with CABP was recently completed comparing DLX (300mg IV/ 450mg PO BID) to moxifloxacin (MOX; 400mg IV/ 400mg PO QD). This analysis includes PORT Risk Class III-V.

Methods

Multicenter, randomized, double-blind trial of adults with CABP with ≥ 2 clinical symptoms: cough, sputum, dyspnea, and chest pain; physical signs; and radiographic evidence of pneumonia. Patients were randomized 1:1 to DLX or MOX treatment for 5-10 days (3 days IV minimum, then oral at investigator discretion). Primary clinical endpoint was the investigator assessed response at Test of Cure (TOC) 5-10 days after last dose. Clinical success was defined as complete/near resolution of signs and symptoms and no further antibiotics needed. Among secondary endpoints, all-cause mortality at Day 28 was assessed.

Results

746 patients were randomized with PORT Risk Class III-V in the Intent-To Treat (ITT) population: 60.5% male; mean age 61.5 yrs (23.9% \geq age 75); 30.7% were PORT class IV-V; 30.1% multi-lobar pneumonia; 55% with CrCl < 90 mL/min. Overall bacterial pathogens were identified in 60.7% at baseline. Patients received mean 8.5 days of DLX (6.4/2.1 days of IV/oral) compared to 8.6 days of MOX (6.4/2.2 days of IV/oral). Clinical Success at TOC in the ITT was 91.0% (342/376) for DLX vs 89.2% (330/370) for MOX (95% CI: 2.6, 6.2)], and in the Clinically Evaluable population 94.8% (331/349) DLX vs 93.8% (320/341) MOX (95% CI: 2.5, 4.6). All-Cause Mortality at Day 28 was reported in n=8 DLX vs n=6 MOX patients. 14.4% DLX and 12.4% MOX patients had ≥ 1 treatment-related adverse events (AEs). Most common DLX events were mild to moderate diarrhea and transaminase elevations, which did not lead to treatment discontinuation. There were no QT-related AEs in DLX patients; one MOX patient reported QT prolongation.

Conclusions

IV/oral DLX demonstrated comparable efficacy to IV/oral MOX for the treatment of patients with moderate to severe CABP (PORT class III-V). DLX confirmed its favourable safety and tolerability profile without the potential for QT prolongation, phototoxicity, or major drug-drug interactions.

4 OR

An Open label, Dose-finding, Pharmacokinetics (PK), Safety and Tolerability Study of a Single Dose Infusion of Meropenem-Vaborbactam (MV) in Pediatric Subjects from age 2 to Less Than 18 Years of Age

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Background

Vabomere® is a fixed combination of meropenem/vaborbactam, approved for the treatment of complicated urinary tract infections in adults, including infections due to *Klebsiella pneumoniae* Carbapenemase (KPC)-producing Enterobacteriaceae. In a phase 1 study in pediatric subjects, the PK objective is to achieve a PK exposure profile comparable to adults.

Methods

This is a Phase 1 open-label, PK, safety and tolerability trial of a single IV dose of MV in pediatric subjects from birth to less than 18y. Subjects were already receiving systemic antibiotics for treatment of suspected or confirmed bacterial infection or peri-operative prophylactic use of antibiotics. PK samples were obtained at 3, 4 and 6 hours after the start of the single 3-hour infusion of MV. In Cohorts 1 and 2A, MV were each dosed at 40 mg/kg. After the independent safety monitoring board review, it was decided to increase the dose for Cohort 3 to 60 mg/kg each of MV and add 4 additional subjects at this dose as Cohort 2B. Max dose in all cohorts was 2g/2g MV. Subjects were evaluated for safety through Day 7. PK and safety data from the first 3 cohorts are presented.

Results

Twenty-eight subjects in the first three age cohorts (12 to <18y, 6 to <12y, and 2 to <6y) have completed the study. MV was well tolerated and all patients completed the 3 hr infusion. There were no serious adverse events (AEs) reported; 8 patients reported treatment emergent AEs and 3 patients reported AEs possibly related to study drug. PK in children age 2 to less than 18y is compared to adult data from the Phase 3 studies.

Conclusions

MV was well tolerated in all ages tested to date. The single dose PK profile for subjects aged 12 to less than 18y with 40 mg/kg each of MV and aged 2 to less than 6y with 60mg/kg each of MV was comparable to a single 2g/2g MV IV dose in adults. Further study is needed in the age 6 to less than 12y age group.

5 OR FRS

Impact of antimicrobial stewardship education using a de-identified, provider-specific prescribing scorecard on outpatient antibiotic prescribing practices

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Background

Inappropriate antibiotic prescribing is the most important risk factor leading to antibiotic resistance. A previous evaluation of antibiotic prescribing at Saint Francis Hospital and Medical Center (SFHMC) identified sub-optimal prescribing for respiratory infections, urinary tract infections (UTIs), and skin and soft tissue infections (SSTIs) in the outpatient setting. In response, clinic pharmacists provided education to attending physicians using a de-identified provider-specific prescribing scorecard and antibiotic prescribing algorithms for the above indications. The purpose of this study is to assess the impact of this intervention on outpatient antibiotic prescribing.

Methods

This study was reviewed and approved by the Institutional Review Board at SFHMC. Outpatient antibiotic prescription data and medical records were reviewed for patients in adult primary care and continuity care clinics between July 1, 2017 to June 30, 2018 (pre-intervention) and April 1, 2019 and September 30, 2019 (post-intervention). Patient demographics, antibiotic prescriptions, indication, prescribing provider and drug allergies were collected. Investigators determined appropriate drug choice and duration of therapy based on the documented indication, drug allergies and clinical practice guidelines. The primary outcome was the rate of inappropriate antibiotic prescriptions for respiratory infections, SSTIs and UTIs before and after providing education with the de-identified provider-specific prescribing scorecard.

Results

The rate of inappropriate antibiotic prescriptions for respiratory infections, SSTIs and UTIs combined was reduced from 74% to 56% following education with the de-identified prescriber scorecard ($p < 0.001$). This improvement was largely driven by reductions in inappropriate prescribing for SSTIs (97% pre-intervention, 67% post-intervention, $p < 0.001$) and UTIs (60% pre-intervention, 19% post-intervention, $p = 0.002$). Inappropriate prescribing rates for respiratory infections were unchanged (66% pre-intervention, 61% post-intervention, $p = 0.699$).

Conclusions

A one-time educational intervention using a de-identified provider-specific prescribing scorecard led to an 18.4% decrease in the rate of inappropriate antibiotic prescriptions for the three most common indications studied: respiratory infections, SSTIs, and UTIs. Use of a de-identified prescriber scorecard in providing stewardship education is effective in reducing inappropriate antibiotic prescribing in an outpatient setting where ongoing stewardship resources are limited; however, additional strategies may be needed to drive and sustain further improvement in antimicrobial prescribing.

6 OR

Perceptions of Antimicrobial Stewardship Among Pharmacy Students and Faculty

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Background

Antimicrobial stewardship is a growing field of interest in many healthcare professions, including pharmacy. There have been data to suggest that pharmacists practicing in the community setting may not use these principles as often in the workplace as those employed in an institutional setting. The purpose of this study was to assess the perceptions of antimicrobial stewardship based on pharmacy practice setting, interest in infectious diseases, and anticipation of postgraduate training.

Methods

This was a cross-sectional study conducted using an online survey instrument. The survey was distributed via email to pharmacy students (professional years 1-4) and faculty at D'Youville School of Pharmacy. Data collected included demographics, career interests, and 29 survey questions using a 5-point Likert scale. Descriptive statistics were used for demographic data. A Chi-square or Fisher's exact test were used as appropriate to assess differences in positive agreement (agree/strongly agree) for each survey question. Faculty and student perceptions were analyzed based on practice setting (institutional, outpatient, or no practice setting). Perceptions based on interest in infectious disease (yes or no) and anticipation of postgraduate training (yes or no) were assessed only among students.

Results

The survey had a usable response rate of 22.9% (n=58). The mean (standard deviation) age of the participants was 29.4 (11.6) years. There were no significant differences between the practice settings for any of the survey questions. Thirty (96.8%) students interested in infectious diseases agreed that antimicrobial stewardship interventions can have an impact on antimicrobial resistance rates in community settings (p=0.017). Twenty (83.3%) students who anticipated postgraduate training agreed that antibiotics are overused in institutional settings (p=0.049).

Conclusions

There were no differences in perceptions of antimicrobial stewardship across the different pharmacy practice settings. Students' academic interests and career aspirations may influence their perceptions of antimicrobial stewardship.

7 OR FRS

Effects of a symptom-driven urinary algorithm on urine screening and antibiotic utilization

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Background

Urine cultures are often obtained when symptoms of a urine tract infection are absent. Consequences of treating asymptomatic bacteriuria (ASB) are increased symptomatic recurrence, increased prevalence of antibiotic resistant organisms, and a longer duration of hospitalization in those that are hospitalized at the time of testing. Several studies have shown that implementation of diagnostic stewardship efforts, including requiring indications for urine cultures and limiting automatic urinalysis (UA) reflex to cultures leads to a significant decrease in number of urine cultures, catheter-associated urinary tract infections (CAUTI), and days of therapy (DOT).

Methods

This was a multi-center, pre- and post-implementation, quasi-experimental analysis performed at Novant Health. In May 2018 interventions made to urine culture processing included updating the urinalysis criteria, implementing symptom-driven urinalysis evaluation panel, and updating the overall urinary algorithm. The primary endpoint was CAUTI rates pre-implementation versus post-implementation. Secondary endpoints included: the number of UAs, urine cultures, urinary tract infections (UTIs), and antibiotic days of therapy (DOT).

Results

Pre-implementation there were 0.185 CAUTIs per 1000 patient days compared to 0.113 post-implementation ($p < 0.001$). There was also a decrease in UAs per 1000 patient days from 76.64 to 70.75 ($p = 0.027$). There was an insignificant increase in the number of urine cultures per patient days from 36.73 to 37.76 ($p = 0.17$) and urinary tract infections per patient days from 2.45 to 2.59 ($p = 0.20$). Overall, there was a decrease in the antibiotic days of therapy (DOT) for patients with a UTI from an average of 1434.27 per month pre-implementation to 1291.25 per month post-implementation ($p < 0.001$).

Conclusions

Changes to the system wide urinary algorithm resulted in a significant decrease in CAUTI rates. The reduction in the number of UAs performed without a subsequent reduction in urine cultures and UTIs suggests that the symptom-driven urinary algorithm resulted in more appropriate ordering of UAs. These efforts to reduce the treatment of ASB and other antimicrobial stewardship efforts to improve appropriate duration of therapy resulted in a significant reduction in antibiotic DOTs for those diagnosed with a UTI.

Cost-effectiveness analysis of new beta-lactam beta-lactamase inhibitor antibiotics versus colistin for the treatment of carbapenem-resistant infections

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Background

Carbapenem-resistant enterobacteriaceae (CRE) present a serious public health problem because of high mortality rates and limited treatment options. The standard treatment for CRE infections has been colistin and polymyxin B which are associated with high rates of acute kidney injury (AKI). Since 2014, four new beta-lactam beta-lactamase inhibitor (BLBLI) combinations have been approved for this indication. Due to the emergent need for new antibiotics for CRE, most of these antibiotics were approved based on small studies. The price of a treatment course of these new BLBLI are over ten times as expensive as colistin. The goal of this study was to evaluate the cost-effectiveness of the new BLBLIs compared to colistin for the treatment of CRE.

Methods

A systematic review of the literature was completed. Studies were included if they were randomized controlled trials or cohort studies in which BLBLIs were compared to colistin. Outcome data was incorporated into a cohort-level decision tree model of the treatment of CRE. The primary outcomes included quality-adjusted life years (QALYs) and incremental cost-effectiveness ratio (ICER). Model inputs included: clinical outcomes and events (28-day mortality and AKI), cost of treatment and adverse drug events and health utilities. A 3% discount was applied for costs and outcomes beyond the first year. A lifetime horizon was used from the perspective of the US healthcare system with a willingness-to-pay (WTP) threshold of \$100,000. A one-way sensitivity analysis was done to incorporate uncertainty.

Results

Assuming 1000 simulations per intervention, the BLBLI group cost, on average, \$15,500 and produced 11.5 QALYs per patient. The colistin group cost \$3,500 and produced 8.0 QALYs per patient. The ICER for the new BLBLIs compared to colistin was \$3,400 per QALY gained, which is cost-effective at the specified WTP threshold. The ICER result was most impacted by uncertainty in the cost of an AKI, the relative risk of mortality, and the health utility associated with survival. Treatment with a new BLBLI remained cost-effective under all tested sensitivity analyses.

Conclusions

New BLBLIs are cost-effective compared to colistin for the treatment of CRE and are associated with improved mortality and fewer AKI events. The use of colistin should be reserved for cases where new BLBLIs are not available or there is documented resistance to these new antibiotics.

Eight Years of Sustained Potency and Activity of Oritavancin against Gram-Positive Isolates Causing Bacteremia and Endocarditis in the USA, including Enterococcal Infections

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Background

Oritavancin (ORI) is a potent lipoglycopeptide with desirable PK/PD parameters for treating serious gram-positive infections. This study assessed the activity of ORI against *Staphylococcus aureus* (SA), *Enterococcus faecalis* (EF), and *E. faecium* (EFM) causing bloodstream infection (BSI), including infective endocarditis (IE) and daptomycin (DAP)-susceptible dose-dependent (SDD) vancomycin-resistant (VRE) subsets. We also evaluated the longitudinal activity of ORI.

Methods

A total of 5,469 SA, 1,157 EF, and 721 EFM were recovered from BSI in 35 US sites (2011-2018). Subsets of SA isolates causing IE (84) and EFM displaying DAP-SDD-VRE phenotypes (230) were included. Identification was confirmed by MALDI-TOF MS and isolates were tested for susceptibility (S) according to CLSI.

Results

Overall, ORI showed similar MIC₅₀ (0.03 mg/L) and MIC₉₀ results (0.06 mg/L) against MRSA and MSSA and the SA IE subset (41.7% MRSA). Similar findings were noted for ORI tested against EF DAP-S (MIC_{50/90}, 0.015/0.06 mg/L) and DAP-SDD (MIC_{50/90}, 0.015/0.06 mg/L). ORI MIC values against DAP- and VAN-S EFM (MIC_{50/90}, ≤0.008/0.015 mg/L) were at least 8-fold lower than those from DAP-SDD-VRE isolates (MIC_{50/90}, 0.06/0.12 mg/L; 31.9% of all EFM), and all EFM were inhibited by ORI at ≤0.25 mg/L. The longitudinal analysis showed MRSA rates varying from 39.7% (2017) to 46.8% (2011), while the annual ORI MIC₅₀ and MIC₉₀ results were 0.015-0.06 mg/L and 0.03-0.12 mg/L, respectively, against MRSA during the 8-year period. ORI yearly MIC₅₀ and MIC₉₀ results were 0.015-0.03 mg/L and 0.03-0.12 mg/L against EF, respectively. MIC₅₀ and MIC₉₀ results of 0.008-0.03 mg/L and 0.03-0.12 mg/L, respectively, were obtained for ORI against the DAP-SDD EF subset each year. ORI MIC₅₀ and MIC₉₀ results of 0.03-0.06 and 0.06-0.12 mg/L were obtained annually against DAP-SDD-VRE (EFM), respectively.

Conclusions

ORI showed a potent activity against this collection of isolates causing BSI and IE in the USA, including resistant subsets requiring higher dosage regimens when treating serious infections. In addition, ORI maintained a stable potency throughout the 8-year study period with no apparent temporal trends.

10 OR FRS

Impact of Audit-and-feedback on the Incidence of Acute Kidney Injury in Adults Receiving Piperacillin-Tazobactam and Vancomycin

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Background

Piperacillin-tazobactam and vancomycin (PT/VAN) is a combination commonly used as empiric antimicrobial therapy in hospitalized patients. Recent studies have suggested an association between PT/VAN and increased incidence of acute kidney injury (AKI). Our study aimed to determine whether an antimicrobial stewardship intervention could reduce the incidence of AKI in patients receiving PT/VAN.

Methods

A quasi-experimental pre-post intervention study was conducted in a 772-bed teaching hospital. Patients who received PT/VAN for at least 48 hours between February and October 2019 were included. The intervention consisted of an “audit and feedback” note in the patient file as well as a continuous educational strategy. The incidence of AKI, defined by the KDIGO guidelines, was the primary outcome. Promptness of de-escalation as well as overall consumption of PT/VAN and other broad-spectrum antibiotics were also assessed.

Results

125 patients were included (72 and 53 in the pre-intervention and intervention groups, respectively). In the intervention group, 14 patients (26.4%) had AKI before onset of PT/VAN versus 20 patients (28.8%) in the pre-intervention group. Among the remaining patients, 7 (17.9%) from the intervention group and 13 (25.0%) from the pre-intervention group developed AKI during the 10 following days. A survival analysis comparing the incidence of AKI between the two groups was not statistically significant ($p=0.45$). However, de-escalation at 48 hours was significantly higher in the intervention group (45.3% versus 23.6% in the pre-intervention group, $p=0.009$). On average, de-escalation occurred after 3.24 days of PT/VAN in the intervention group, and after 3.97 days in the pre-intervention group ($p=0.049$). In both groups, the most frequent type of de-escalation was discontinuation of vancomycin only. There was no increase in consumption of other broad-spectrum antibiotics. Mortality rates (11.3% in the intervention group versus 15.3%, $p=0.60$) as well as median length of stay (17.6 days in the intervention group versus 22.6, $p=0.18$) were similar in both groups.

Conclusions

A PT/VAN focused audit and feedback had a significant impact on time to de-escalation in patients receiving PT/VAN as an empiric combination. Despite no significant impact on AKI and increasing evidence of lack of association between PT/VAN and AKI, the intervention was maintained as part of our hospital’s stewardship program.

11 OR FRS

Evaluation of a pharmacy stewardship initiative on antibiotic discharge prescribing

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Background

2.8 million antibiotic-resistant infections occur in the United States annually. Overtreatment of established infection drives antibiotic resistance and increases risk of complications, such as *Clostridioides difficile* infection. Ensuring optimal duration of therapy is important in antimicrobial stewardship initiatives. The purpose of this study was to evaluate a pharmacy antibiotic stewardship initiative to change duration of therapy by altering discharge prescription defaults. The primary outcome was to assess the impact of this initiative on duration of therapy by calculating the duration error for each prescription. Secondary outcomes included assessment of errors related to antimicrobial selection, dose, and frequency.

Methods

The electronic medical record (EMR) was utilized to identify patients discharged from the hospital that received an electronic prescription for studied antibiotics. Patients who met inclusion criteria had their antibiotic discharge prescriptions retrospectively reviewed by the investigator. Patients were randomly selected from the data source until 150 patients were selected from both the pre-intervention and post-intervention time frames. Fifty patients in each group were assessed for antibiotics that had default duration reduced to 7 days (group A). Another 50 patients in each group assessed the removal of the defaulted duration (group B). The final 50 patients in each group served as a reference group (group C). Inclusion criteria: Patients discharged from our study locations ≥ 18 years of age and that received an electronic discharge prescription for 1 or more studied antibiotics. Exclusion Criteria: An infection without clearly defined duration of therapy recommendations, or receipt of an infectious disease consult during hospitalization.

Results

In group A, outpatient antibiotic average days prescribed decreased 0.8 days, incorrect duration prescribing decreased 10%, and average duration error decreased by 1.3 days. In group B, outpatient antibiotic average days prescribed decreased 3.5 days, incorrect duration prescribing decreased 24%, and average duration error decreased by 4.4 days. In group C, outpatient antibiotic average days prescribed decreased 1.2 days, incorrect duration prescribing decreased 4%, and average duration error decreased by 1.4 days.

Conclusions

An antimicrobial stewardship initiative demonstrated the biggest impact when antibiotic default durations were removed in the EMR. Further evaluation with a larger patient population and long-term assessment of outcome data would be beneficial for extrapolation and identification of result applicability.

12 OR FRS

The use of area under the curve to determine therapeutic vancomycin dosing in skin and soft tissue infections

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Background

The vancomycin AUC/MIC target ratio of 400 to 600 mg*h/L that is recommended (level IA+) in the 2020 IDSA/ASHP vancomycin TDM guidelines is appropriate for patients with complicated MRSA infections; using lower targets for less complicated infections may reduce the risk for nephrotoxicity without compromising efficacy. The current methodology surrounding vancomycin AUC/MIC targets is a “one size fits all” policy, in which source specific targets are not identified, especially for relatively lower risk MRSA infections such as skin and soft tissue infections (SSTIs). To our knowledge, studies defining the optimal AUC/MIC ratio for SSTIs have not been performed.

Methods

This was a retrospective observational study of hospitalized patients at the Veterans Affairs Health Care System in San Diego, CA with a SSTI and prescribed intravenous vancomycin between January 1, 2017 and December 31, 2018. Patients included were adults, 18 years of age and older, treated with IV vancomycin with ≥ 1 measured concentration for at least one of the ICD-10 CM codes for SSTI. Patients were excluded if they had any of the following SSTIs: (1) osteomyelitis; (2) infection related to chronic ulcers or wounds; (3) SSTI involving the face, eye, mouth, ear, or nose; (4) peri-rectal SSTI; (5) human or animal bite SSTI; (6) SSTI related to retained foreign body; (7) necrotizing SSTI; (8) surgical site infection/post-operative infection. Patients were also excluded if they were undergoing dialysis or had severe immunosuppression. Clinical and pharmacokinetic information was used to determine the lowest vancomycin AUC threshold associated with clinical cure.

Results

A total of 378 patients on vancomycin for a SSTI were identified from the database query for screening, and 149 (39.4%) met inclusion criteria for the study. The median age of the 149 patients studied was 63 (range 27-92) years. Of the 229 excluded patients, the most common reason for exclusion was osteomyelitis (76 patients, 20.1%). Classification and Regression Tree (CART) modeling identified a calculated AUC of >179 as having the highest correlation with clinical success (not statistically significant). 91.8% of the 147 patients with calculated AUCs of >179 had clinical success. For patients with an AUC of ≤ 179 (n=2), only 50% had clinical success. The median length of hospital admission was 5 days. The average vancomycin duration of therapy was 4 ± 1 days. Staphylococcus aureus was recovered in 51 patients (34.2%), of which 24 (16.1%) were MRSA and 27 (18.1%) were MSSA. All of the S. aureus isolates had a vancomycin MIC ≤ 1 mg/L. Nephrotoxicity occurred in 3 (2%) of patients. Of those 3 patients, 1 had an AUC of 575 and trough of 22.6.

Conclusions

Based on a high percentage of responders with an AUC below the recommended range of 400-600, we suggest that patients may be exposed to more vancomycin than necessary when the current guideline recommendations are followed. To determine if there is overexposure, and the margin of overexposure, more data will need to be captured. Our sample size was calculated a priori to be 120 subjects with 60 in each arm to achieve a power of 80%. Based on our power analysis, more data is needed to further define a statistically significant AUC range. Expanding the time frame of this study to include more patients will help to discern whether this trend towards a lower AUC range for SSTIs holds true.

13 OR FRS

Comparative Incidence of Acute Kidney Injury in Septic Patients Treated with Vancomycin in Combination with Piperacillin/Tazobactam vs. Cefepime

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Background

Empiric antibiotic therapy for patients who present with sepsis of unknown origin is typically broad spectrum and includes coverage for *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA). Nephrotoxicity is a well-established adverse event of IV vancomycin, and recent literature suggests that combination with piperacillin/tazobactam may increase risk for incidence of acute kidney injury (AKI) as compared to combination with other beta-lactam antibiotics. However, evidence is conflicting thus far. The primary outcome of this study was to compare the incidence of AKI in septic patients who received IV vancomycin in combination with piperacillin/tazobactam (VZ) vs. cefepime (VC). Secondary outcomes include hospital length of stay, inpatient mortality, and impact to direct variable cost.

Methods

Adult patients who were discharged with a sepsis diagnosis code and received VZ or VC for ≥ 24 hours in 2012-2019 were retrospectively identified and evaluated. AKI was defined using RIFLE criteria. Patients were excluded for ESRD on HD, AKI occurring < 48 hours after treatment initiation or > 7 days after discontinuation, pregnancy, febrile neutropenia, or meningitis. Statistical analysis controlled for several factors including age, race, gender, Elixhauser comorbidity burden, hours to first antibiotic dose, length of stay, and receipt of concomitant nephrotoxins.

Results

A total of 12,405 patients were evaluated; 7,818 received VZ and 3,097 received VC. Patients who received VC demonstrated a 40% reduction in the risk of experiencing AKI compared to those who received VZ (IRR 0.600; 95% CI 0.46-0.78). These patients also demonstrated a 4% reduction in risk of having one additional inpatient day (IRR 0.961; 95% CI 0.937-0.985). Patients who received VZ and experienced AKI were 82.3% more also likely to die while hospitalized compared to patients that did not receive VZ and did not experience AKI (IRR 1.822; 95% CI 1.50-2.21). Finally, patients treated with VC incurred significantly less in direct variable cost on average than those treated with VZ ($p = 0.034$) and those who suffered an AKI also incurred significantly more on average than those without AKI ($p = 0.005$).

Conclusions

Compared to septic patients treated with VZ, those treated with VC had a significantly decreased risk of experiencing an AKI as defined by the RIFLE criteria. Patients who received VZ were at higher risk for a longer hospital length of stay and, if they also experienced an AKI, inpatient mortality. VZ was associated with higher direct variable cost and patients with AKI incurred more dollars per encounter than those without AKI.

14 OR FRS

Out with the Old, In with the New? In Vitro Susceptibility Comparison of Tetracyclines Against Carbapenem-resistant Enterobacterales

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Background

Carbapenem-resistant Enterobacterales (CRE) are an emerging problem world-wide. Recently, novel agents in the tetracycline class, eravacycline and omadacycline, have been developed to combat the increasing antimicrobial resistance in bacteria. However, susceptibility data directly comparing the activity of the novel tetracyclines and previous tetracyclines are lacking. An evaluation of CRE in vitro susceptibility to eravacycline, omadacycline, tigecycline, and minocycline was conducted at an academic medical center in Indianapolis, Indiana.

Methods

CRE isolates were collected and stored from a time period of 2015 to 2019 at our institution. Minimum inhibitory concentrations (MIC) to minocycline, tigecycline, omadacycline, and eravacycline were determined by Etests (bioMérieux) or MIC Test Strips (Liofilchem). Susceptibility was determined using breakpoints established by the U.S. Food & Drug Administration (FDA), European Committee on Antimicrobial Susceptibility Testing (EUCAST), and the Clinical Laboratory Standards Institute (CLSI).

Results

Twenty-seven CRE isolates were comprised of *Klebsiella pneumoniae* (78%), *Serratia marcescens* (11%), *Enterobacter cloacae* (7%), and *Enterobacter aerogenes* (4%). With a susceptibility breakpoint of a MIC \leq 0.5 mcg/mL (EUCAST) or a MIC \leq 2 mcg/mL (FDA), overall tigecycline susceptibility ranged from 4% to 96%, respectively. Overall minocycline susceptibility was 78% using a susceptibility breakpoint of a MIC \leq 4 mcg/mL (FDA/CLSI). Overall omadacycline susceptibility was 48% using a susceptibility breakpoint of a MIC \leq 4 mcg/mL (FDA). Eravacycline proved to have the highest overall susceptibility of 100% using a breakpoint of a MIC \leq 0.5 mcg/mL (FDA/EUCAST).

Conclusions

According to the current FDA-approved susceptibility breakpoints, previous tetracyclines have similar or more in vitro activity against our CRE isolates compared to the novel agents of the class. Overall, eravacycline proved to be the most potent tetracycline against twenty-seven CRE isolates at an academic medical center in Indianapolis, Indiana.

15 OR FRS

Evaluation of Outcomes Associated With Intermittent Versus Extended Infusion of Piperacillin/tazobactam in Acutely Ill Veterans

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Background A key principle of antimicrobial stewardship is the optimization of antibiotic dosing. Many institutions have implemented dosing protocols for extended-infusion of beta-lactams as a stewardship initiative. This study will evaluate the impact of an extended-infusion piperacillin/tazobactam dosing protocol on clinical outcomes in acutely ill veterans treated for infections at VA San Diego.

Methods This single-center, retrospective cohort study looked at veterans admitted to the medical-surgical unit who were treated with piperacillin/tazobactam for at least 48 hours. The control group included patients who received treatment between 12/14/2017 to 7/22/2018, and the “protocol” or after protocol implementation group included patients who received treatment between 7/23/2018 to 2/28/2019. Excluded from the study were veterans with microbiological cultures showing intermediate sensitivity or resistance to piperacillin/tazobactam, those who experienced interruption in therapy, or those who required hemodialysis or peritoneal dialysis. Demographic and selected clinical information were collected to describe the groups. Primary clinical outcomes included in-hospital mortality rate, 30-day mortality rate, hospital length of stay (LOS), and 30-day readmission rates. Rates of adverse effects such as elevated liver enzymes, thrombocytopenia, acute kidney impairment (AKI), and *Clostridium difficile* infection were also collected. SPSS Statistics was used to perform χ^2 tests and Fisher’s exact tests for nominal data, and Mann-Whitney U tests for non-parametric continuous data.

Results 260 veterans were included in the final analysis: 96% male, mean age 65 ± 13 years, 84 met SIRS criteria for sepsis (33.8% control vs. 30.8% protocol group), and majority concurrently received another antibiotic (72.3% control vs. 66.9% protocol group). For primary outcomes: median LOS was 7 days for the control vs. 6 days for the protocol group ($p=0.15$), in-hospital mortality occurred in 0.8% of the control vs. 0% of the protocol group ($p=1.00$), 30-day mortality occurred in 3.8% of each group, and 30-day readmission occurred in 20.8% of the control vs. 13.1% of the protocol group ($p=0.23$). There was a statistically significant difference in incidence of AKI which occurred in 56.9% of the control vs. 39.2% of the protocol group ($p=0.004$). There were no statistically significant differences in secondary outcomes of incidence of liver enzyme elevation (39.2% vs. 28.5%, $p=0.17$), thrombocytopenia (26.2% vs. 22.3%, $p=0.47$), and *Clostridium difficile* infection (3.1% vs. 1.5%, $p=0.684$). For veterans who received at least 48 hours of concomitant vancomycin, 63.2% of the control vs. 42.3% of the protocol group developed AKI ($p=0.011$). In veterans with obesity, 70.8% of the control vs. 36.4% of the protocol group developed AKI ($p=0.001$).

Conclusions There were no statistically significant differences in primary clinical outcomes between veterans who received intermittent or extended-infusion dosing of piperacillin/tazobactam. There was a statistically significant lower rate of AKI with extended-infusion dosing, which was also demonstrated in subgroup analyses for veterans who received concomitant vancomycin and veterans with obesity. The results of this study support the enhanced patient safety achieved by extended-infusion dosing of piperacillin/tazobactam. Contrary to previous studies, extended-infusion dosing was shown to significantly reduce rates of AKI in patients with concomitant vancomycin therapy.

16 OR FRS

National survey of ambulatory antimicrobial stewardship practice

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Background

Antimicrobial stewardship programs (ASPs) are effective in improving patient care and minimizing inappropriate antibiotic use. As a result, The Joint Commission published new standards requiring ASPs in the ambulatory setting starting January 2020. However, guidance for implementing effective strategies in the ambulatory setting is lacking. This study describes the current state of ambulatory antimicrobial stewardship in a national cohort of health-system affiliated settings and serves as a benchmark for strategies that may be associated with effectiveness.

Methods

This was a cross-sectional, multi-center, national survey study. Participant responses were summarized using descriptive statistics. Inferential comparisons were analyzed using Chi-squared or Fisher's exact test for nominal data, as appropriate, and the Mann-Whitney U test for continuous non-parametric data.

Results

129 unique survey responses from a variety of institution types across 44 states were received. Survey respondents reported a fully functioning ASP in 9/129 (7%) of ambulatory practices compared to 114/129 (88%) of inpatient institutions ($P<.001$). Additionally, 100/129 (78%) expressed interest in or current development of ambulatory ASP. For the Core Elements of Outpatient Stewardship, 35/129 (27%) reported meeting Commitment, 33/129 (26%) Action/Policy, 45/129 (35%) Tracking/Reporting, and 43/129 (33%) Education. Effectiveness in at least 1 outcome (i.e. utilization, resistance, *C. difficile* infection, or cost) in the past 2 years was measured and reported in 103/124 (83%) of inpatient and 18/100 (18%) of ambulatory ASPs ($P<.001$). Common characteristics of ambulatory ASPs demonstrating effectiveness was dedicated pharmacist support 13/18 (72%), institution guidelines 16/18 (89%), rapid diagnostic testing (RDT) for respiratory viruses or Group A Streptococcus 16/18 (89%), and outpatient antibiograms 14/18 (78%). 16/44 (36%) ambulatory programs with at least 1 Core Element measured and reported effectiveness in the past 2 years, compared to 4/4 (100%) meeting all 4 Core Elements.

Conclusions

Expansion of Antimicrobial Stewardship in the ambulatory setting is imperative to address antibiotic misuse. For programs in development, initial efforts focused on use of institution specific guidelines, RDT, outpatient antibiograms and dedicated pharmacist support may be most impactful for program effectiveness. Following the Centers of Disease Control and Prevention Core Elements should remain foundational for ASP development.

17 OR FRS

Evaluation of penicillin-aminoglycoside and dual β -lactam therapies in Enterococcus infective endocarditis (EIE)

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Background

A first line regimen for EIE caused by penicillin susceptible isolates has historically been the combination of penicillin G or ampicillin with an aminoglycoside (A+G). However, with rates of high levels of resistance to aminoglycosides (HLAR) approaching 50%, there is a need for alternative treatment options. In addition, extended courses of aminoglycosides also carry the risk of nephrotoxicity. Most recently, dual β -lactam (A+C) synergistic activity has been demonstrated by the mechanism of binding different penicillin binding proteins. The American Heart Association (AHA) infective endocarditis treatment guidelines include A+C therapy as a first line regimen for EIE. The purpose of this study is to compare rates of treatment modifications and failures among individuals treated with A+G versus A+C therapies for EIE.

Methods

This is a retrospective, single-center cohort study of adult patients with ampicillin susceptible Enterococcus endocarditis and receipt of A+G or A+C therapy for at least 48 hours between July 2009 and July 2019. Individuals were excluded if they had a polymicrobial infection, experienced death within 48 hours of admission, were pregnant, and/or had relapsed infection. The primary outcome was rate of adverse events (i.e., nephrotoxicity, ototoxicity, allergic reaction) requiring treatment modification. Secondary outcomes included rate of any event requiring treatment modification and rate of treatment failure which was a composite of mortality during treatment, relapse, and persistent infection requiring treatment modification.

Results

A total of 63 individuals with EIE that received A+G (19 patients) or A+C (44 patients) therapy were included. Baseline characteristics between groups were similar. Most individuals had community-acquired endocarditis caused by Enterococcus faecalis from an unknown source (68.3%). Rates of adverse events requiring treatment modifications were 52.6% in A+G and 15.9% in A+C group ($p = 0.003$). Renal toxicity was the most common reason for treatment modification in A+G group (83.3%). The incidence of AKI defined by RIFLE criteria was 36.8% in A+G versus 11.4% in A+C group ($p = 0.018$). Rates of any event requiring treatment modifications were 63.2% in A+G and 22.7% in A+C group ($p = 0.002$). Treatment failure was observed in 21.1% in A+G and 27.3% in A+C group ($p = 0.757$).

Conclusions

In patients with EIE, A+G therapy was associated with greater frequency of treatment modification, especially related to nephrotoxicity. An A+C regimen may provide a tolerable and equally efficacious option for treatment of EIE in adults and confirms the AHA guideline recommendation.

18 OR FRS

Evaluation of outpatient antibiotic prescribing for acute otitis media (AOM) in pediatric patients 2 months to 18 years old

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Background

Treatment guidelines for AOM in pediatric patients provide differing recommendations for initial management. Antimicrobial therapy and watchful waiting are outlined as appropriate options. Core Elements of Outpatient Antibiotic Stewardship, developed by Centers for Disease Control and Prevention, recognizes delayed antimicrobial prescribing and watchful waiting for mild AOM. These approaches can safely decrease antimicrobial use, adverse events, and development of resistance. The purpose of this evaluation is to characterize the appropriateness of antimicrobial prescribing for AOM in pediatric patients according to current guideline recommendations.

Methods

This evaluation is a retrospective, observational, cross-sectional design of pediatric patients who were diagnosed with AOM between July 2018 and July 2019 at a pediatric outpatient facility. A random sample was stratified in a 4:2:1 ratio by clinic location and month of visit. Patients were excluded if they had recurrent AOM and/or receipt of non-systemic antimicrobials.

Results

A total of 168 individuals diagnosed with AOM during the time frame were included. Antibiotics were prescribed in 99.4% of cases, of which 80.8% were inappropriate based on deviation from current guideline recommendations of agent, dose, and/or duration. The median antibiotic duration was 10 days. Shorter durations were ideal for 59.8% of individuals. Penicillin antibiotics were the most prescribed (80.3%) at a median dose of 76.5 mg/kg/day. One individual was managed with delayed prescribing approach, although 63.7% were eligible based on clinical factors. Three patients (1.8%) were classified as treatment failures.

Conclusions

In pediatric patients with AOM, the majority received suboptimal antibiotic therapy. Extended treatment durations and inadequate dosing were the most common reasons for inappropriateness. There was a lack of delayed prescribing, although many individuals met clinical criteria for this approach. A small percentage of patients experienced treatment failure, potentially highlighting the effectiveness of standard dose penicillin and/or unnecessary antibiotic utilization for this indication.

A Novel Program to Deliver Outpatient Parenteral Antibiotic Therapy and Drug Recovery Assistance in People Who Inject Drugs

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Background

Hospitalizations for serious bacterial infections (SBI) have markedly increased in people who inject drugs (PWID). Standard of care for many SBI conditions includes long-term outpatient parenteral antimicrobial therapy (OPAT). Behavioral challenges including risk of overdose or central line abuse preclude safe hospital discharge on OPAT. Historically, this issue frequently led to either extremely prolonged hospitalizations or patients leaving against medical advice on substandard antibiotic treatment. Here we describe a novel partnership between four Intermountain Healthcare hospitals and a non-profit residential detoxification facility to provide simultaneous drug recovery assistance (DRA) and OPAT.

Methods

The DRA-OPAT program was evaluated using a pre-post study design. We compared outcomes in PWID hospitalized with SBI who were candidates for program participation during a 1-year post-implementation period (2018) with similar patients from a historical control period (2017), identified by propensity modeling and manual review.

Results

Eighty-seven hospitalized patients were candidates for DRA-OPAT in the implementation period, with 35 participants (40.2%) discharged to the community-partner facility; of these 16 (45.7%) completed the full OPAT duration. Patients with similar characteristics were identified as a pre-implementation control group (n=51). Median length of stay was reduced from 22.9 days (IQR 9.8-42.7) to 10.6 days (IQR 6-17.4) after program implementation, p<0.0001. Total median cost was also decreased from \$39,220.90 (IQR \$23,300.71-\$82,506.66) pre-implementation to \$27,592.39 (IQR \$18509.45-48369.11) post-implementation, p<0.0001. Readmission rates at 90 days were similar (23.5% vs 24.1%), p=0.8. At 1-year follow-up, all-cause mortality was 7.1% in the pre-implementation group vs 1.2%, p=0.06.

Conclusions

Creative partnerships between hospitals and community resources hold promise for providing resource-efficient OPAT and drug recovery assistance. We observed significant reductions in length of stay and cost without increases in readmission rates; 1-year mortality may have been improved. Further study is needed to optimize benefits of the program.

20 OR FRS

An Evaluation of Empiric Antipseudomonal Dosing on the Incidence of Treatment Failure

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Background

Pseudomonas aeruginosa (*P. aeruginosa*) is a pathogen associated with significant mortality, attributed to a delay in appropriate antibiotic therapy secondary to antibiotic activity and/or timeliness. However, the impact of dosing on clinical outcomes has been largely unreported. Our study evaluated treatment failure as it related to empiric antipseudomonal antibiotic dosing in patients with culture-positive *P. aeruginosa*.

Methods

This retrospective cohort compared the incidence of treatment failure in patients with documented *P. aeruginosa* receiving guideline-concordant (GC) or guideline-discordant (GD) empiric therapy with cefepime, meropenem, or piperacillin/tazobactam. Patients with culture-positive *P. aeruginosa* between July 1, 2013 and July 31, 2019 were eligible for inclusion. Patients with cystic fibrosis, polymicrobial infections, and potential urinary tract or pulmonary colonization were excluded. The primary outcome was treatment failure, defined as a composite outcome of 1) Increased or unchanged qSOFA score 48 hours after initiating therapy, 2) Persistent fever (>38°C) 48 hours after initiating therapy, or 3) Therapy modification due to resistance or perceived treatment failure. Secondary outcomes included frequency of infectious diseases (ID) consultation, all-cause inpatient mortality, mechanical ventilation requirement, as well as infection-related, ICU, and hospital length of stay.

Results

198 patients were included – 90 GC patients and 108 GD patients. Baseline characteristics were balanced between groups. Treatment failure was more common in the GD than the GC group (62% vs. 48%; p=0.04). The primary outcome remained significant when adjusting for suprathreshold dosing regimens (64% vs. 48%; p=0.02). Frequency of ID consultation was significantly higher in the GD group (46% vs. 29%, p=0.01), while length of ICU stay was significantly longer in the GC group (4.5 days vs. 3 days, p=0.03). Additional secondary outcomes did not vary significantly between groups.

Conclusions

Treatment failure was significantly higher in patients receiving guideline-discordant empiric antipseudomonal dosing. Guideline-directed empiric antipseudomonal dosing, specific disease states, and patient-specific factors should be taken into account when considering the dose for empiric antipseudomonal coverage.

21 OR FRS

Isavuconazole for Prophylaxis and Treatment of Invasive Fungal Infections in Immunocompromised Adults

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Background

Patients with hematologic malignancies or those receiving immunosuppressive agents, such as sirolimus or tacrolimus, for graft-versus-host disease prophylaxis following stem-cell and solid organ transplantation have an increased risk of developing serious invasive fungal infections (IFI). Triazole antifungal agents are commonly utilized for IFI prophylaxis during periods of prolonged neutropenia. Isavuconazole is FDA approved for the treatment of invasive aspergillosis and mucormycosis, but its role in antifungal prophylaxis has not been fully elucidated. Due to its broad spectrum of activity, favorable safety profile, and linear pharmacokinetics, isavuconazole for IFI prophylaxis has been implemented across many clinical institutions, despite minimal clinical data to support its use.

Methods

We conducted a single center, retrospective review of all hospitalized patients who received at least one dose of isavuconazole therapy during January 1, 2018 to August 31, 2019. Subjects that met the requirements for the study were obtained from the electronic medical record. Breakthrough invasive fungal infections were identified according to the EORTC/MSG criteria.

Results

A total of 20 patients were included for evaluation. The average length of therapy was 11.5 days (range, 1-71). The majority of patients had acute myeloid leukemia (70%) and the remainder of patients had another hematologic malignancy (25%) or solid organ transplant (5%). Three patients underwent allogeneic hematopoietic stem cell transplant. Twelve patients received isavuconazole for treatment while eight patients received prophylaxis. All patients received an appropriate loading dose for treatment, however, 6 out of 8 patients did not receive a loading dose for prophylaxis. Twenty-five percent of patients receiving isavuconazole for prophylaxis developed proven or probable breakthrough infection.

Conclusions

The rate of breakthrough infection was found to be higher than those reported in the literature (10-15%). Furthermore, there were no proven breakthrough IFI in patients who received a loading dose for prophylaxis, which suggests that a loading dose may be needed to attain adequate isavuconazole concentration and efficacy. Our results support the current literature which report consistent breakthrough infections with isavuconazole prophylaxis. Randomized controlled trials are needed to identify the relationship between the administration of prophylactic loading doses and breakthrough infection rates.

Real-world utilization of eravacycline in the outpatient setting

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Background

Eravacycline (ERV) is a fully-synthetic, fluorocycline antibacterial with activity against Gram-negative, Gram-positive aerobic and anaerobic pathogens. ERV was FDA-approved in 2018 for the treatment of complicated intra-abdominal infections in patients ≥ 18 years of age. Outpatient Parental Antimicrobial Therapy (OPAT) services have been widely adopted across the United States and can offer potential benefits to patients and health-systems. In this study, we describe ERV real-world utilization and evaluate the clinical and safety outcomes in patients treated with ERV in the outpatient setting.

Methods

A multicenter retrospective study included patients treated at OPAT facilities across the United States between October 2018 and February 2020. Patients who received ≥ 1 dose(s) of ERV were included. Data captured patient demographics, comorbidities, risk factors, diagnosis, baseline pathogens, and ERV regimen. Outcomes and adverse events (AE) were collected. The primary objective was to describe the clinical utilization of ERV in the real-world outpatient setting. Secondary objectives were to evaluate clinical, microbiological and safety outcomes of patients treated with ERV using pre-defined criteria.

Results

19 patient cases were collected from OPAT facilities. Patient demographics consisted of 57.9% (11/19) male, median age 56 (range, 31-80) years, mean weight 110.1 (range, 57-216) kg and mean Charlson Comorbidity Index of 3 (range, 0-8). 94.7% (18/19) of patients had comorbid conditions and 68.4% (13/19) had risk factors for resistant organisms attributed to recent hospitalization and antibiotic exposure. Sources of infection were intra-abdominal (10/19), skin and soft tissue (6/19) and other (3/19). 15 baseline pathogens were reported in 10 patients, most commonly Enterococcus spp. (n=3), methicillin-resistant Staphylococcus aureus (n=2), Escherichia coli (n=2) and Acinetobacter baumannii (n=2). Mean ERV duration was 24 (range, 4-73) days and 89.5% (17/19) of patients received antimicrobial therapy prior to ERV. ERV was administered at 1 mg/kg q12hr or 1.5 mg/kg q24hr in 10/19 and 9/19 patients, respectively. Clinical cure, defined as complete resolution of signs and symptoms with no additional antibiotics required end of ERV therapy, was achieved in 12/19 (63.2%) cases; 1/19 (5.2%) had clinical improvement. There were 6/19 (31.6%) with clinical failure, including 3 who discontinued ERV due to AEs. Overall, 4/19 (21%) patients experienced AEs, most commonly were GI-related events and rash. Notably, no cases of Clostridioides difficile infection were reported.

Conclusions

Clinical cure was achieved in the majority of ERV treated patients and was generally well-tolerated. Additional investigation is warranted to fully determine the potential benefits of ERV in this treatment setting.

Efficacy of Bacteriophage-Antibiotic Combinations on Two Different Phenotypes of Methicillin-resistant *Staphylococcus aureus*

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Background

The widespread use of antibiotics has generated selective pressures that have driven the emergence of multi-drug resistant strains. The antimicrobial of choice for invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections has been vancomycin; however, treatment failures have continued to be reported secondary to poor drug performance or the development of various resistant phenotypes. Bacteriophages (phages) have been suggested as a potential adjunctive/alternative therapy. These phages exhibit bactericidal activity by infecting bacterial cells, redirecting the cellular machinery to produce progeny virions and killing the bacterial cell upon lysis and release of those progeny phages. *Staphylococcus aureus* naturally releases extracellular vesicles (EVs) during growth, which are known to play important functions in bacteria-bacteria interactions and potentially transferring antibiotic resistance genes. Unfortunately, there is limited data on the use of phage-antibiotic combinations and bacterial response to these. The objective of this study was to test the in-vitro activity of various standard of care (SOC) antibiotics with phages and their effects on EVs formation.

Methods

Phage-antibiotic exposure was tested on two different phenotypes of MRSA, isolates MW2 (daptomycin non-susceptible) and D712 (vancomycin intermediate resistant *S. aureus*). Phage, bacterial counts and EVs formations were performed during time-kill analysis (TKA) experiments. MRSA isolates were examined against an array of antibiotics alone (daptomycin, vancomycin, ceftaroline and cefazolin) and in combination with phages. Bacteriophage Sb-1 was used for experiments at $\sim 10^5$ PFU/ml. Bactericidal activity was defined as a $>3 \log_{10}$ CFU/ml reduction from baseline. Synergy between two agents was defined as a $>2 \log_{10}$ CFU/ml reduction at 24 hours compared to either agent alone.

Results

In vitro 24-hour TKA experiments demonstrated bactericidal activity with phage-antibiotic combinations. While addition of ceftaroline or cefazolin to vancomycin or daptomycin was synergistic, both daptomycin-phage and vancomycin-phage combinations resulted in bactericidal activity against the D712 strain. In addition, emergence of EVs in presence of phages was suppressed in antibiotic-phage combination regimens for both MRSA isolates.

Conclusions

The combination of antibiotic-phages showed promising results against MRSA. If shown to be reproducible in vivo, this phenomenon would be valuable in the treatment of clinical cases that are treatment refractory or have failed SOC antibiotics.

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Comparison of Short Versus Long Durations of Oral Cephalosporin Therapy for Pyelonephritis

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Background

Evidence regarding shorter treatment durations of oral cephalosporins for uncomplicated pyelonephritis is limited. The purpose of this study was to evaluate the outcomes of short versus long durations of oral cephalosporins in the emergency department (ED) and ambulatory clinics at Carilion Clinic.

Methods

This retrospective non-inferiority cohort included adult females presenting to any ED, urgent care, or outpatient office for pyelonephritis and treated with an oral cephalosporin for short (7 to 9 days) or long (10 to 14 days) durations from January 1, 2017 to December 31, 2018. Exclusion criteria were age \leq 18 years, urologic abnormality, catheter use within 14 days, pregnant, immunosuppression, cirrhosis, or an absolute neutrophil count $< 500/\mu\text{L}$. A non-inferiority margin of 0.15 was selected to detect a difference in the primary endpoint of treatment failure at 30 days. Secondary outcomes were all-cause admissions, infection-related admissions, *Clostridioides difficile* infection, and development of an MDR pathogen within 90 days.

Results

Treatment failure at 30 days occurred in 10.3% of the patients in the short group and in 4.1% of the patients in the long group ($p=0.15$). Of the 184 patients, 181 (98.3%) received cephalexin, ranging from doses of 250-500 mg two to four times daily. Patients receiving longer durations were more likely to receive a one-time initial dose of ceftriaxone (20.7% vs. 53.6%, $p<0.001$) and were more likely to visit the emergency department (54% vs. 74.2%, $p=0.0054$). There were no all-cause or infection-related admissions at 30 days and 90 days in either group. There was no difference in *C. difficile* infection within 90 days and no documented development of MDR urinary or blood pathogens.

Conclusions

Short durations of oral cephalosporins were non-inferior to long durations for women with uncomplicated pyelonephritis treated on an outpatient basis.

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Variation of Antimicrobial Use in Emergency Departments within a Large Health System

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Background

The emergency department (ED) is a major setting for antimicrobial prescribing for both the inpatient and outpatient setting. The purpose of this study was to characterize the variability of antimicrobial use across five ED sites within a large health system in order to identify targets for antimicrobial stewardship.

Methods

This was an IRB-exempt, retrospective ecological study that compared antimicrobial use on a population-level at five ED sites from January 1, 2019 to December 31, 2019. Antimicrobial use was measured in the form of days of therapy per 1000 patient-days (DOT). Antimicrobial agents were divided into four categories to further assess antimicrobial use according to the National Healthcare Safety Network definitions: all antimicrobials, antibiotics predominantly used for resistant Gram-positive infections, antibiotics predominantly used for hospital-onset infections, and antibiotics posing the highest risk of *Clostridioides difficile* infection (CDI). ED sites with higher than average antibiotic use will be compared to the sites with average to below average use. Descriptive statistics were used for statistical analysis.

Results

Overall, there were 341,789 ED patient encounters in 2019. In order of most DOT to least DOT, the top ten antibiotics prescribed during 2019 include (average DOT/ED site): ceftriaxone (656), vancomycin (314), azithromycin (285), metronidazole (211), cefepime (167), cephalexin (127), doxycycline (121), piperacillin/tazobactam (116), clindamycin (58) and trimethoprim/sulfamethoxazole (55). The average DOT for all antimicrobials per month for each site was 211 (low 160, high 231). The average DOT for antibiotics predominantly used for resistant Gram-positive infections was 26 per month (low 19, high 30). Within this category, three ED sites had higher than average DOT (28 to 30 DOT vs 26). Next, the average DOT for antibiotics predominantly used for hospital-onset infections was 26 per month (low 16, high 34). Two ED sites had DOT above average consistently within this category (33 to 34 DOT vs 26). Finally, the average DOT for antibiotics posing a high risk for CDI was 80 per month (low 72, high 91). Two ED sites had DOT above average (86 to 91 DOT vs 80).

Conclusions

Trending and comparing antimicrobial use in the ED identified outliers of antimicrobial use for focused antimicrobial stewardship efforts. Further analysis is needed to assess how ED facility characteristics influence antimicrobial prescribing.

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Creation and Evaluation of a Pharmacist-led beta-lactam Allergy Assessment Program at an Academic Medical Center

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Background

The incidence of reported beta-lactam allergy is as high as 15%. Despite the reported allergy, more than 95% of patients evaluated for their allergy have tolerated penicillin and cephalosporin derivatives. Documented allergy to beta-lactam antibiotics leads to the initiation of broad-spectrum and often, suboptimal antibiotics. Compared to targeted therapy, these broad-spectrum antibiotics are associated with increased toxicity, emergence of multi-drug resistant organisms (MDRO), and increased healthcare costs. The primary objective of this study was to evaluate the number of interventions that can be provided by completing a pharmacy-driven allergy assessment program.

Methods

This combined retrospective chart analysis (Phase I and II) and post-implementation cohort analysis (Phase III) included patients who were admitted to pre-specified teams at an academic medical center with a documented beta-lactam allergy. Other inclusion criteria included an active infection wherein beta-lactam antibiotics served as the therapy of choice. The retrospective chart analysis took place from March 1 – April 30, 2019 (Phase I), and November 1 – December 31, 2019 (Phase II). Phase III was conducted from January 1 – February 29, 2020. The number of interventions that could have been provided was assessed in all three phases. Other endpoints such as adherence to protocol, infection with *Clostridioides difficile* and/or MDRO, and length of stay were also measured.

Results

The analysis included 207 patients (64 in Phase I, 73 in Phase II, and 70 in Phase III). Through chart review alone, interventions could have been provided to 27 (42%) patients in Phase I, 34 (46%) patients in Phase II, and 32 (46%) patients in Phase III. Of those interventions, more than 15% qualified to have their reported beta-lactam allergy safely removed from their electronic health record (EHR). Even though completion of pharmacist-led beta-lactam allergy assessment was found to be low, 13% of the patients in Phase III had their allergy safely removed. Length of stay and infection rates with MDRO did not differ between the three phases. Infection rates with *Clostridioides difficile* was significantly higher in Phase I compared to Phase II and III (4.7% vs 0% vs 0%, respectively; $p = 0.03$).

Conclusions

Many patients with reported beta-lactam allergy have clinically insignificant reactions or have previously tolerated a related antibiotic. Pharmacist-led beta-lactam allergy assessment allowed for the safe allergy de-labeling from patients' EHR. However, adherence to protocol was relatively low. Further clarification regarding the low adherence rate and education to clinical pharmacists is required prior to hospital-wide implementation of beta-lactam allergy assessment.

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Impact of Diagnostic and Antimicrobial Stewardship on Time-to-Appropriate Therapy and Clinical Outcomes in Infections caused by Carbapenem-resistant Gram-negative Organisms

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Background

Carbapenem-resistant Gram-negative organisms (CRGNOs) cause life-threatening infections and incidence is rising globally. Timely therapy in these infections has a direct impact on patient survival. We aimed to determine the impact of diagnostic and antimicrobial stewardship (AMS) on time-to-appropriate therapy (TAP) and clinical outcomes of CRGNO infections using novel beta-lactam/beta-lactamase inhibitors (BL/BLIs).

Methods

Retrospective cohort study of adult patients with CRGNO infections at a 1,500-bed University-affiliated hospital. Included patients received ≥ 72 hours of ceftazidime-avibactam (C/A) or ceftolozane-tazobactam (C/T) from 12/2017-10/2019. During the pre-intervention period (12/2017-12/2018), additional susceptibilities (including C/A and C/T) were performed only upon providers' request. In 1/2019, we implemented reflex algorithms for faster identification and testing of all CRGNOs. Results were communicated in real-time to the AMS team to tailor therapy. Benefit-risk outcomes involving TAP, kidney injury, and mortality were evaluated by desirability of outcome ranking (DOOR) analysis.

Results

Ninety-four patients were included with no differences at baseline; median age 61 years (IQR 40.0-68.3), 51 (54.3%) were in intensive care at time of culture collection; median APACHE II score was 20 (IQR 15.0 – 27.0). CRGNOs identified included 71 (75.5%) *Pseudomonas* spp. and 23 (24.5%) Enterobacteriales, of which 16 (17.0%) were carbapenemase producers (KPC=10, NDM=4, VIM=2). The most common infections were pneumonia (47.9%) and bacteremia (26.6%). We found a significant decrease in median TAP (102.9 [IQR 76.0–155.8] vs 75.4 [IQR 56.3–101.2] hours, $p = 0.003$) and length-of-stay (64 [39.9-131.6] vs 43 [20.0-83.8] days; $p = 0.027$). Median time from culture collection to final susceptibility results was shorter in the post-intervention group (122.2 vs 92.4 hours; $p < 0.001$). In multiple regression analysis, our intervention demonstrated a trend towards decreased 30-day inpatient mortality (OR = 0.36, 95% CI 0.13–1.10). The probability of a better DOOR in the post-intervention group was 73.6% (95% CI 71.3–75).

Conclusions

Our study identified improvement in TAP and clinical outcomes in CRGNO infections with implementation of diagnostic and AMS initiatives.

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You need to just stop. Missed stewardship opportunities during pharmacist-driven vancomycin dosing

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Background

Intravenous (IV) vancomycin has been a highly efficacious antimicrobial agent against increasing strains of methicillin-resistant *Staphylococcus aureus*. Due to increased spread of the resistant strains, vancomycin is extensively used empirically in many perceived bacterial infections. Unnecessary and prolonged IV vancomycin exposure can lead to adverse drug events, most notably nephrotoxicity, which may result in prolonged hospital length of stay. The purpose of this study is to identify areas of improvement in antimicrobial stewardship for vancomycin appropriateness by clinical pharmacists at the time of redosing.

Methods

This medication use evaluation was a retrospective, observational cohort study at a large, urban academic medical center. Inclusion criteria was met for patients that received at least three days of IV vancomycin where the clinical pharmacy service assessed for appropriate continuation with a hospital admission between June 19, 2019 and June 30, 2019. Patients less than 18 years old, vancomycin indicated for prophylaxis or administered by routes other than IV were excluded. The primary outcome was to determine the frequency and clinical components of inappropriate vancomycin continuation at the time of redosing. Inappropriate vancomycin continuation was defined as cultures positive for methicillin-susceptible *Staphylococcus aureus*, vancomycin-resistant bacteria, and non-purulent skin and soft tissue infection in the absence of vasopressors. Data was reported using descriptive statistics and measures of central tendency.

Results

Of the 237 patients screened, 119 patients (50.2%) met inclusion criteria. Population characteristics included a mean age of 56 years old, 75 (63%) were male, and 63 (53%) in general practice units (GPU) versus 56 (47%) in intensive care units (ICU). Of those excluded, 24 (20%) were indicated for prophylaxis with a mean duration of 3 days. 49 (48%) patients received vancomycin for 1 day and 53 (52%) for 2 days before discontinuation. The mean duration of vancomycin therapy for all patients was 5 days. Patients in the ICU received vancomycin for 5 days compared to 6 days in the GPU. Vancomycin was continued inappropriately at re-dose in 41% of those assessed.

Conclusions

Vancomycin is used extensively for empiric treatment of presumed infections. Appropriate de-escalation of vancomycin therapy is important to decrease the incidence of adverse effects and to help decrease hospital length of stay. According to the mean duration of therapy, there are opportunities for pharmacy and antibiotic stewardship involvement at the time of redosing.

Improving prescribing practices at hospital discharge with pharmacist-led antimicrobial stewardship at transitions of care

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Background

Antimicrobial stewardship (AMS) is recommended in hospital, post-acute, and outpatient settings. The transitions of care (TOC) are important in each of these settings; however, AMS efforts during TOC have been limited. Beginning in October 2018, we sequentially implemented a pharmacist-led multi-disciplinary review of oral antimicrobial therapy prescribed at hospital discharge from general and specialty medicine wards across a health system. Pharmacists facilitated input of discharge prescriptions following early identification and collaborative discussion of patients to be discharged on oral antimicrobials. The purpose of this study was to evaluate the impact of AMS during TOC.

Methods

This was an IRB-approved stepped-wedge, quasi-experimental study in a 5-hospital health system that included hospitalized adults with skin, urinary, intra-abdominal, and respiratory tract infections discharged from general and specialty wards with oral antimicrobials. Patients with complicated infections, neutropenia, or transferred from an outside hospital were excluded. The primary endpoint was optimization of antimicrobial therapy at time of hospital discharge, defined by correct selection, dose, and duration according to institutional guidance. Outcomes were compared before and after the intervention.

Results

800 patients were included: 400 in the pre-intervention and 400 in the post-intervention period. 252 (63%) received the intervention by a pharmacist per protocol during TOC. Patients had similar comorbid conditions between pre- and post- intervention. Pre-intervention patients were more likely to be discharged from community hospitals. Before intervention, 36% of discharge regimens were considered optimized, compared to 81.5% after the intervention ($p < 0.001$); this was largely driven by reduction in patients receiving a duration of therapy beyond the clinical indication (44.5 vs 10%, $p > 0.001$). There was similar clinical resolution, 30-day readmission, and adverse drug events (ADEs) between pre- and post- periods. Post-discharge antimicrobial duration of therapy was reduced from 4 (3-5) days to 3 (2-4) days ($p < 0.001$). Severe ADEs occurred more frequently in the pre-intervention group (9 vs 3.3%, $p = 0.001$), which was driven by isolation of multidrug-resistant pathogens (7 vs 2.5%, $p = 0.003$) and *Clostridioides difficile* (1.8 vs 0.5%, $p = 0.094$). Patients that received optimal therapy at discharge were less likely to develop an ADE (adjOR 0.530, 95%CI 0.363-0.773).

Conclusions

Implementation of an AMS TOC protocol reduced antimicrobial days, optimized therapy selection and reduced duration. This was associated with improved safety without compromise of clinical effectiveness. To increase patient safety, AMS programs should target antimicrobial optimization during TOC.

Bacteriophage-Antibiotic Combinations for *Enterococcus faecium* with Varying Daptomycin and Bacteriophage Susceptibilities

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Background

Daptomycin (DAP) is a treatment option for serious *Enterococcus faecium* (*E. fcm*) infections. Growing concerns regarding the increased prevalence of DAP-nonsusceptible (DNS) strains necessitate novel therapies. Obligately lytic phages are viruses that target, infect, and kill bacterial cells. Synergistic interactions have been described with phage-antibiotic combinations; however, no study has evaluated these combinations against DNS *E. fcm*, and there are limited studies analyzing membrane vesicle (MV) formation with phage-antibiotic combinations. We sought to determine the ability of combinations of phage plus DAP alone and in addition to DAP plus various beta-lactams (ampicillin: AMP; ceftaroline: CPT; ertapenem: ERT) to improve bacterial killing and alter resistance development of *E. fcm* strains with varying susceptibilities to DAP/phage.

Methods

E. fcm strains R496, R497, and HOU503 were evaluated. Mueller-Hinton broth II (Difco, Detroit, MI) supplemented with 50 mg/L calcium was used for experiments. Minimum inhibitory concentration (MIC) and phage susceptibility were performed, and 24h time-kill analyses (TKA) were conducted at 0.5x and 0.25x MIC, or free peak concentration (whichever was lower). Phage ATCC 19950-B1 was used at an initial phage:bacteria ratio of 0.1 or 1, depending on strain susceptibility. Synergy ($\geq 2\text{-log}_{10}$ CFU/mL kill compared to most effective agent alone at 24 hours) and bactericidal activity ($\geq 3\text{-log}_{10}$ CFU/mL reduction at 24 hours compared to starting inoculum) were evaluated in TKA. MV experiments and evaluation of antibiotic resistance development were performed as previously described.

Results

R496/R497 were DNS; HOU503 was DAP susceptible dose-dependent. R496, HOU503, and R497 exhibited low, medium, and high phage susceptibility, respectively. Against R497, synergistic and bactericidal effects were seen with DAP-AMP-phage and DAP-CPT-phage, while DAP-ERT-phage exhibited synergy. Synergistic effects were noted with DAP-CPT-phage and DAP-ERT-phage (compared to antibiotic combinations) with HOU503. No enhancement was noted with phage addition to antibiotics against R496. There were no significant differences in vesicle formation. No DAP resistance emerged with R496/R497; MICs of HOU503 increased for all regimens except DAP-AMP-phage.

Conclusions

Our results highlight the importance of phage-to-strain specificity contributing to synergy with antibiotics. Further in vitro and in vivo research are needed.

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Evaluation of *Clostridioides difficile* management in the ambulatory setting

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Background

Approximately 34% of adult *Clostridioides difficile* infections (CDI) are community associated with possibly many more under-diagnosed or under-reported. While many health systems have developed inpatient antimicrobial stewardship programs (ASPs) to help optimize CDI care, little information is available regarding community associated CDIs managed in ambulatory care. Outpatient ASPs in the United States has largely focused on improving antibiotic prescribing by targeting specific conditions (e.g. upper respiratory tract, otitis media, pharyngitis) for improvement. An opportunity exists for outpatient ASPs to optimize CDI prescribing strategies within this setting. We evaluated the management of CDI in the outpatient setting.

Methods

This study was an IRB approved, retrospective cross-sectional study to evaluate the management of patients diagnosed with a first episode of CDI in an ambulatory care setting between January 1, 2018 and June 31, 2019. Patients included were 18 years or older, had a clinical diagnosis of *C. difficile* infection, and treatment initiated by the ambulatory clinic. Exclusion criteria were patients with severe CDI, fulminant CDI, immunocompromised patients, or patients who had a fecal microbiota transplant. The primary outcome of this study was to characterize the management of *C. difficile* infections for patients in the ambulatory setting. Secondary outcomes will evaluate the impact of ambulatory *C. difficile* infections management on patient safety and recurrence of infection. Appropriate management was defined as vancomycin 125 mg by mouth every 6 hours for 10-14 days per national practice guidelines. Metronidazole 500 mg by mouth every 8 hours for 10-14 days was considered appropriate if was prescribed as an alternative for cost, allergy, or limited resource availability. Data were analyzed using descriptive statistics.

Results

A total 126 patients were identified with CDI diagnosed in an ambulatory clinic. Median age was 58 years [IQR, 46-69] and 73% were female; the clinic most frequently visited was internal medicine (n = 50, 39.7%), followed by specialty (n = 46, 36.5%), family medicine (n = 24, 19%), and walk-in (n = 6, 4.8%). 49 (38.9%) had documented prior antibiotic exposure within 60 days. Metronidazole (n = 82, 65%) was prescribed most often, followed by vancomycin (n = 40, 32%). 4 (3%) patients received either ciprofloxacin or ciprofloxacin and metronidazole for treatment. Overall, 38 (30%) of patients were prescribed the appropriate antimicrobial therapy and duration. 26 (20.6%) patients, clinical response did not occur with the prescribed regimen. Of those, 23 (n = 26; 88%) were prescribed inappropriate treatment. Overall, 10 (8%) patients had unanticipated emergency department or urgent care visits within 14 days post treatment initiation relating to CDI; 6 of 10 (60%) were prescribed inappropriate treatment. 27 (21.4%) patients experienced rCDI. Of those, 18 patients (n = 27; 67%) received inappropriate therapy.

Conclusions

Ambulatory CDI treatment may represent a missed opportunity for institutional ASPs to minimize associated morbidity. A focused effort is needed to improve the quality of CDI management in outpatient setting.

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A retrospective evaluation to determine if area underneath the concentration-time curve-guided vancomycin dosing impacts the incidence of acute kidney injury associated with piperacillin- tazobactam

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Background

Recent studies concluded that the combination of piperacillin-tazobactam (P/T) and vancomycin increases the risk for acute kidney injury (AKI). The purpose of this study was to determine if an area underneath the concentration-time curve- (AUC) guided vancomycin dosing strategy reduced the incidence of AKI in patients that received vancomycin plus P/T.

Methods

This was a retrospective, pre-post quasi-experimental study comparing the incidence of AKI before and after a health-system-wide change from trough- to AUC-guided vancomycin dosing using 2 post- distribution levels. Included patients were hospitalized, at least 18 years of age, and received at least 3 consecutive calendar days of vancomycin. The most common reasons for exclusion were unstable renal function on initiation, meningitis indication, or a trough goal other than 15-20 mg/L. The primary outcome was AKI, defined as an increase in serum creatinine of ≥ 0.5 mg/dL or 50% from baseline for 2 consecutive measurements, in patients that received vancomycin and at least one concomitant dose of P/T.

Results

A total of 636 patients were included (308 trough-guided; 328 AUC-guided) and of those, 118 patients in each group received concomitant P/T. Baseline characteristics between the trough- and AUC-guided groups were similar for age (59.7 vs 59.5 years), initial total daily dose (2,131 vs 2,140 mg), and initial trough (12.9 vs 12.0 mg/L), but significantly different for body weight (78.4 vs 94.4 kg; $p < 0.0001$) and body mass index (27 vs 31.8 m/kg²; $p = 0.007$), respectively. AKI associated with vancomycin plus P/T occurred in 21/118 (17.8%) patients in the trough-guided group versus 16/118 (13.6%) patients the AUC-guided group ($p = 0.803$). The incidence of AKI was significantly higher in patients that received concomitant P/T versus no concomitant P/T in both the trough-guided group (21/118 [17.8%] vs 14/190 [7.4%], respectively; $p = 0.003$) and AUC-guided group (16/118 [13.6%] vs 8/210 [3.8%], respectively; $p = 0.0011$).

Conclusions

The incidence of AKI in patients that received vancomycin plus P/T did not significantly differ between trough and AUC-guided vancomycin dosing. The incidence of AKI was significantly higher when P/T was administered with vancomycin regardless of dosing strategy. Caution should be taken when combining vancomycin and P/T. Further studies are needed to confirm these findings.

Antibiotic penetration and bioavailability of vancomycin alone and in combination with rifampin in *Staphylococcus epidermidis* biofilms

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Background

Despite frequent clinical use, a research gap exists regarding the efficacy and interplay of rifampin combination therapy for staphylococcal prosthetic joint infections (PJIs). Questions remain regarding the potential formation of a vancomycin-rifampin molecular complex that may hinder penetration through biofilm matrixes. Our lab's previous time-kill results utilizing combination vancomycin + rifampin, identified persister cells after 48 hours of antibiotic pressure. Penetration and bioavailability of vancomycin alone, and with rifampin must be determined to elucidate interactions within biofilms.

Methods

S. epidermidis isolate ATCC® 35984, a known biofilm forming bacteria, was grown on polyurethane coupons and stained with FilmTracer™ Sypro® biofilm matrix stain. Simulated humanized concentrations of BODIPY-vancomycin (BODIPY-van) (25 µg/mL) ± rifampin (1.4 µg/mL) were added to biofilm samples and observed over 60 minutes with confocal fluorescence microscopy. Drug diffusion rate was quantified as mean fluorescence intensity (FI) over time with color histograms. Fluorescence recovery after photobleaching (FRAP) was performed at three depths within the biofilm to determine antibiotic bioavailability.

Results

Mean FI increased over 60 minutes in biofilms treated with both BODIPY-van and BODIPY-van + rifampin but max FI intensity was greater and more rapidly achieved in biofilms treated with BODIPY-van alone (mean max FI: 22.71, 8.19 respectively). Generation of a FRAP curve revealed partial fluorescence recovery for BODIPY-van + rifampin and BODIPY-van at three depths within the biofilm (BODIPY-van + rifampin lower layer: 24%, middle layer: 32%, and upper layer: 36%, and BODIPY-van lower layer: 42%, middle layer: 48%, and upper layer: 48%).

Conclusions

Antibiotic diffusion and bioavailability were reduced for BODIPY-van ± rifampin in *S. epidermidis* biofilms. The addition of rifampin did not improve vancomycin penetration. These data may explain the presence of persister cells identified in time-kill studies with vancomycin + rifampin, that were not observed with vancomycin alone. Further investigation into the molecular interactions with rifampin and other antibiotics, as well as the role of rifampin for biofilm associated PJIs is warranted.

Assessment of Antimicrobial Prescribing Practice and Culture in a Quaternary Care Teaching Hospital

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Background

Antimicrobial resistance (AR) is one of the most critical threats to Global Health. One of its root causes, misuse of antibiotics, can stem from prescribers' preconceived ideas, differing attitudes and lack of knowledge. Canadian data on this subject is scarce. This study aimed to understand the culture of antimicrobial prescribing in order to optimize strategies targeting prescribers in the local antimicrobial stewardship program (ASP).

Methods

An anonymous online survey was distributed to antimicrobials prescribers at a 772 beds acute-care teaching hospital to conduct a prospective cross-sectional study.

Results

240 respondents completed the survey (CI: 95%, MOE: 5.47%). Participation amongst attending physicians, residents and specialized nurse practitioners was 16%, 37% and 29%, respectively. All agreed that AR is a significant challenge in Canada. However, only 46% of respondents believed that antibiotics are misused locally. Most (93%) agreed that ASPs can decrease AR. Several knowledge gaps were identified through clinical questions: for examples, respondents failed to identify treatment indications for asymptomatic bacteriuria 25% of the time, 61% chose an unnecessarily broad antibiotic when presented a susceptibility report from a common clinical situation, and only 28% identified an appropriate length of therapy. Prescribers' confidence did not correlate with knowledge. Number of correct knowledge questions appears to decrease with years of practice ($p < 0.01$). Overall, respondents felt more confident when to start antimicrobial therapy (88%) than when to stop it (62%), yet 29% did not know where to find hospital resources for optimal antimicrobial prescribing.

Conclusions

Respondents recognized AR as a critical issue but awareness and knowledge on antibiotic misuse were lacking. Our results are consistent with prior similar surveys published globally. Barriers to optimal antimicrobial prescribing were identified and strategies for improving the effectiveness of the ASP will be developed accordingly.

Microbial etiology of prosthetic joint infections: What's growing in the cultures?

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Background

Prosthetic joint infections (PJIs) are a tremendous burden for patients and healthcare systems. The Veterans Health Administration is the largest healthcare system in the United States of America (USA), and is comprised of over 170 medical centers. The objective of this study was to describe the organisms isolated from patients diagnosed with PJIs across this national healthcare system.

Methods

Our retrospective cohort study included patients with a diagnosis code for prosthetic joint infection between January 2016 and December 2018 who were admitted to a Veterans Affairs (VA) hospital. Cultures obtained from one day prior to admission through date of discharge were included. Cultures were only included if the site of culture could be specifically attributed to a joint and may have included more than one organism.

Results

We identified 692 positive joint cultures from 3,660 admissions among 2,216 unique patients. The sources of cultures were from the knee (78%), hip (17%), and other/unspecified joint site (6%). Only 7.9% (n=55) of all cultures were polymicrobial. *Staphylococcus aureus* was the most frequently identified organism (49%, n=339), followed by other staphylococci (22%, n=153), and streptococci (12%, n=83). Methicillin resistance was identified in 27% (n=92) of the *S. aureus* isolates, and the majority of methicillin-resistant *S. aureus* (76%, n=70) were isolated from the knee. Gram-negative organisms were identified in 18% (n=123) of all cultures and *Pseudomonas aeruginosa* was the most frequently implicated gram-negative organism (23%, n=28).

Conclusions

Prior studies have reported coagulase-negative staphylococci to be the most common pathogens in PJI, but our study found that *S. aureus* was the most frequently isolated organism in the largest healthcare system in the USA. While gram-positive pathogens are more commonly associated with PJI and are targeted in surgical prophylaxis, gram-negative organisms were present in 18% of cultures, which is concerning due to increasing virulence and antimicrobial resistance.

Impact of Antimicrobial Stewardship on Provider Prescribing Habits for Suspected Urinary Tract Infections in a Community Dwelling Homebound Population

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Background

Antimicrobial stewardship (AS) has been well documented to improve the use of antimicrobials, while decreasing resistance and adverse effects, and improving patient outcomes. There is, though, little guidance for AS within the community. The most common infections treated in the ambulatory care setting are urinary tract infections (UTIs). One study determined that more than 50% of antibiotics prescribed for presumed UTIs were considered unnecessary or inappropriate. The Summa House Calls Program (SHCP) services adult patients who qualify for nursing facility care but have chosen to stay in their homes. UTIs are common in this population, and family members may request antibiotics based on change in mental status or functional decline alone. This study of pre and post design provided AS services to the providers of the SHCP specific to the treatment of presumed UTIs.

Methods

AS interventions included implementation of an interview algorithm for use by the medical assistants, delivery of patient, family, prescriber, and home care nurse education, and AS services provided by a specialized pharmacist for 7 months total. Pre-data was collected for 3 months prior to AS services and education, and post-data was collected for 3 months after. The primary outcome was appropriateness of antibiotic use. Secondary outcomes included number of asymptomatic bacteriuria cases, antibiotic duration, emergency department (ED) and hospital visits, repeat requests for treatment, incidence of *Clostridioides difficile*, urinalysis and urine cultures ordered, AS consultations, and a prescriber knowledge/attitude survey.

Results

A total of 137 patient encounters were included, 54 in the pre and 83 in the post-intervention arm. Appropriate antibiotic usage increased from 51.9% in the pre-intervention arm to 71.1% in the post-intervention arm ($p=0.022$). There was a significant reduction in 30-day ED visits in the post-intervention arm (1.2% vs. 9.3%, $p=0.035$). There were no significant differences in demographics or other secondary outcomes. The post-intervention provider survey demonstrated 100% of the 5 providers were very comfortable/comfortable in assessing the need for antibiotics for UTIs, in selecting and prescribing the most appropriate antibiotic, and when providing the patient/family with educational material regarding UTIs/treatment.

Conclusions

As intervention delivered to providers of a community dwelling homebound population resulted in a significant increase in appropriate antibiotic utilization for the treatment of UTIs.

Aeromonas Hydrophila Infection in an Immunocompetent Patient Leading to Necrotizing Fasciitis

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Background

Aeromonas hydrophila is a heterotrophic gram-negative rod mainly found in areas with a warm climate but can be found in fresh and brackish water. Infection is spread via fecal-oral transmission during direct ingestion or drinking of contaminated water or foods. Infection can also be transmitted by eating contaminated meat, dairy, shrimp, or fish. One of the diseases it can cause in humans, gastroenteritis, occurs mostly in young children and people who are immunocompromised or have growth problems. *Aeromonas hydrophila* is also associated with cellulitis. And in some cases, necrotizing fasciitis has also been reported.

Methods

77 YO female with PMH of DM, A fib and recent H/O ascending cholangitis and cholecystectomy was admitted to our hospital for severe right lower extremity pain. Almost about 2 weeks after the discharge she started to develop sudden onset of right leg pain. Along with that she was also having increased Shortness of breath. In the hospital she was found to be hypotensive, hypoxic and tachycardic. Labs work were done which showed increased WBC count to 29.8 K/uL, with band of 11 and lactic acid of 1.9. Patient was started on IV antibiotics meropenem, vancomycin and metronidazole. Because of the pain in the leg there was a suspicion of DVT so the duplex was done which ruled out DVT, because of her critical condition she was then sent to our hospital for management in the ICU. with the IV fluid as well patient BP was on lower side so was started on norepinephrine drip. On examination of her right leg she was found to have few bullae, was cold to touch, crepitation was present and there was no pulse. so, emergent CT scan of the leg was done which showed features of necrotizing fasciitis. General surgery was consulted and was taken for amputation. Later tissue culture came positive for *Aeromonas hydrophila*.

Results

Infection by *Aeromonas hydrophila* is from feco oral route and can cause gastroenteritis. In some cases, it can cause cellulitis and necrotizing fasciitis. There has been some case report of necrotizing fasciitis caused by *Aeromonas hydrophila*. In one case patient got necrotizing fasciitis after getting wound infection from direct contact with brackish water. there was another case report of fulminant necrotizing fasciitis from *A hydrophila* that was not associated with trauma, liver disease, or immunosuppression. Our case is also somewhat like the second case, patient did not have any trauma and was not immunocompromised and was not exposed to contaminated water. The only thing our patient had was diarrhea which was c. diff positive, but one can argue that it could have been caused by *Aeromonas hydrophila* and C diff was just the colonizer. there has case report on *A. hydrophila* causing necrotizing fasciitis after surgery, including PCI. There is one retrospectively reviewed study which showed that necrotizing fasciitis caused by *A. hydrophila* is more rapidly progressive than cause by *K. Pneumoniae*. Which in turn emphasis on getting surgical intervention as soon as possible

Conclusions

Necrotizing fasciitis caused by *A hydrophila* is a rare entity but is a serious condition and prompt treatment is required. Previously was thought to occur in immunocompromised patient now is being seen on immunocompetent patient as well. as seen in our case can be preceded by diarrhea as well, and one must be vigilant enough to diagnose these conditions.

38 OR FRS

Fecal Microbiota Transplantation vs. Fidaxomicin or Oral Vancomycin for the Treatment of Recurrent *Clostridioides difficile* Infection

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Background

Clostridioides difficile infections are one of the most common healthcare-associated infections in the United States. The IDSA guideline recommended treatment for initial *Clostridioides difficile* infections is either vancomycin or fidaxomicin. Although antibiotic therapy is effective, treatment with oral vancomycin and fidaxomicin is associated with a 25% and 15% infection recurrence rate, respectively. Recurrent *Clostridioides difficile* infections have even higher rates of infection recurrence when treated with antibiotics. Additionally, there is limited data on the effectiveness of antibiotics in patients with recurrent infections, especially in patients with more than one recurrence. Fecal microbiota transplantation (FMT) is a non-FDA approved, experimental procedure that has the highest level of evidence for treating patients with multiple recurrent *Clostridioides difficile* infections; however, there is limited data comparing antibiotic therapy to FMT.

Methods

Data was collected retrospectively from a single-center electronic medical record database. Patients were included if they were at least 18 years of age and had a recurrent *Clostridioides difficile* infection that was treated with oral vancomycin, fidaxomicin, or FMT. Patients were excluded if they were less than 18 years of age, pregnant, immunocompromised (e.g. HIV, chemotherapy, etc.), or received antibiotics within 10 weeks following treatment of a recurrent *Clostridioides difficile* infection. The primary efficacy outcome of the study was recurrence within 10 weeks following the end of treatment. The secondary efficacy outcomes were global cure at 10 weeks and recurrence at 5 weeks following the end of treatment.

Results

A total of 81 patients were included for analysis. Recurrent *Clostridioides difficile* infections within 10 weeks after treatment occurred in 2 of 27 FMT patients, 3 of 27 fidaxomicin patients, and 8 of 27 oral vancomycin patients. No difference in recurrent infections was found when comparing FMT to either fidaxomicin (7.41% vs. 11.11%; $p = 0.076$) or oral vancomycin (7.41% vs. 11.11%; $p = 0.076$). Global cure at 10 weeks following treatment occurred in 24 of 27 FMT patients, 18 of 27 fidaxomicin patients, and 15 of 27 oral vancomycin patients. Patients who received FMT had a higher incidence of global cure when compared to oral vancomycin (88.89% vs. 55.56%; $p = 0.024$), but not when compared to fidaxomicin (88.89% vs. 66.67%; $p = 0.099$).

Conclusions

The use of FMT was not found to have a significantly lower number of recurrent infections when compared to either fidaxomicin or oral vancomycin. When considering the overall outcomes of therapy, patients receiving FMT had a significantly higher rate of global cure than patients receiving oral vancomycin but not fidaxomicin. Additional studies with a larger sample size are needed to determine if FMT treatment has less recurrent infections than oral vancomycin or fidaxomicin.

**Decolonization Strategies and MRSA Infection Rates in a Neurosurgical ICU
at an Academic Medical Center**

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Background

Hospital-acquired infections (HAI) are a significant source of morbidity and mortality. MRSA decolonization upon admission is used by many institutions to reduce infections, but the best strategy to minimize inappropriate antimicrobial use and HAI is still unclear. The 2013 REDUCE-MRSA trial demonstrated that universal decolonization with chlorhexidine baths and mupirocin was superior in preventing both MRSA and all-organism bloodstream infections (BSIs) when compared to targeted decolonization and screening with isolation. Subsequent trials and meta-analyses have displayed benefits in both surgical and nonsurgical patients. The goal of this evaluation was to characterize the decolonization practices as well as MRSA and BSI infection rates in a neurocritical care population.

Methods

This retrospective cohort evaluation included a random sample of admissions to the neurosurgical ICU service from July 2014 to May 2018. 152 unique patients were included with 188 total ICU admissions. Data collected included baseline demographics and comorbidities (including history of MRSA infections), MRSA nares swab result on admission, decolonization strategies, and all procedures, lines, drains, and airways (LDAs) during ICU admission. Additionally, we identified cultures with MRSA identified and all BSI collected from day 3 of ICU admission until day 2 after discharge. BSI with commensal organisms was only documented if two consistent positive cultures resulted.

Results

Six categories of decolonization were identified as followed: mupirocin (29%), chlorhexidine gluconate (CHG) bath alone (4%), non-CHG bath alone (11%), mupirocin + CHG bath (25%), mupirocin + non-CHG bath (24%), and no decolonization (6%). Five patients were diagnosed with HAIs: 3 MRSA and two BSIs (MRSA infection rate = 2.0%). Two infections occurred in the mupirocin only group and mupirocin with non-CHG bath, with 1 in the mupirocin plus CHG bath. Two patients of 152 tested had positive MRSA nares surveillance and received mupirocin + CHG or non-CHG baths; neither developed a HAI.

Conclusions

Despite a small sample size, the rate of MRSA infection was consistent with a large 10-year cohort study in a similar population. Documentation of decolonization methods was inconsistent. We recommend unit or institutional development of a more protocolized approach to decolonization implementation and documentation. Given the low rate of surveillance with positive results and unclear impact of decolonization in a neurosurgical population, further research is warranted to identify potential benefits and costs of decolonization practices.

Clinical Burden of Recurrent *Clostridioides Difficile* Infection in the Medicare Population

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Background

Clostridioides difficile infection (CDI), especially recurrent CDI (rCDI), is associated with high morbidity and resource utilization, and the burden is particularly high for older patients. This study evaluated procedures and complications after CDI, in patients with and without recurrence(s), in the Medicare population.

Methods

A retrospective analysis of claims data from the 100% Fee-for-Service (FFS) Medicare database was performed. Patients with a CDI episode requiring inpatient stay (diagnosis codes: ICD-9-CM 008.45; ICD-10-CM A04.7, A04.71, or A04.72) or an outpatient CDI visit with CDI treatment were identified between January 2010 and December 2016. Included patients were continually enrolled in Medicare Part A, B, and D for 12 months before and 12 months after index episode. Each CDI episode was followed by a 14-day period with no CDI claims after the end of treatment, thus distinguishing rCDI from continuous CDI. rCDI was defined as another CDI episode within an 8-week window immediately after the claim-free period. Procedures and complications were captured over 12 months of follow-up and stratified by number of rCDI episodes.

Results

268,762 patients with an index CDI episode were included. 175,554 (65.3%) did not experience a recurrence, 38,163 (14.2%) had 1 recurrence, 22,898 (8.5%) had 2 recurrences, and 32,147 (12.0%) had 3 or more recurrences within 12 months post-index CDI episode. In comparison to the overall Medicare FFS cohort, those with CDI were older (78.3 yr vs 75.4 yr) and had higher Charlson Comorbidity Index (CCI) scores (5.1 vs 4.0). During a 12-month pre-index period, 84% across all cohorts received antibiotics, and approximately half received gastric acid-suppressing agents. 6-month pre-index hospitalization and ED exposures were highest among individuals with ≥ 3 recurrences. During the 12-month follow-up, approximately 6% of patients with rCDI underwent subtotal colectomy and approximately 1% underwent diverting loop ileostomy. Sepsis occurred during follow-up in 47,382 (27.0%) patients with no recurrence, compared to 33,120 (35.5%) of those with one or more recurrences. During follow-up, incident psychiatric conditions were observed in a notable proportion of patients with CDI or rCDI, with the highest incidence observed for depression (range: 15.3% to 18.2%). Fecal microbiota transplant was performed in 1% of all patients with CDI.

Conclusions

Baseline exposure to antibiotics and hospitalization were highest for those with 3 or more CDI recurrences. Sepsis was observed in over 1/3 of rCDI patients, and appears to increase in a parallel fashion with rCDI episodes. It is important to recognize the significant burden of CDI and rCDI on patients, which can lead to poor quality of life. Prevention of rCDI is a necessary step to reduce the burden of this disease and related complications.

Clarithromycin induced acute transient psychosis in a young healthy adult male

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Background

Used for many infectious processes, clarithromycin is a relatively new macrolide antibiotic advantageous for its dynamic dosing schedule and antimicrobial spectrum. Side effects include gastrointestinal pain, hepatotoxicity, QT prolongation, and rarely altered mental status causing hallucinations and delirium. Herewith, we present a case report on clarithromycin-induced psychosis on an otherwise healthy Eastern European male to raise the awareness of medication side effects early to avoid exacerbation of illness.

Methods

A 33-year-old male presented with altered mental status. A bidaily course of clarithromycin was prescribed to him to treat community-acquired pneumonia by his general practitioner. Two days after use, he hallucinated voices which commanded him to cheat on his wife and perform dance moves. He denied suicidal ideation or homicidal ideation and was negative for thought disorganization, catatonia, visual hallucinations, or nightmares in his psychiatric examination. His physical exam was non-contributory. He had a euthymic mood, normal motor speed, speech, thought process, and orientation.

Results

All laboratory tests were normal except for a high ALT and AST of 569 and 360, respectively, and a low ALP. CRP was elevated at 3.0. Electrocardiogram showed sinus tachycardia. CT chest showed tree-in-bud appearance with nodular opacities in the subpleural lower lobe. CT abdomen showed hepatic steatosis with enlarged mediastinal lymph nodes. CT head was unremarkable. Abdominal ultrasound showed a contracted gallbladder with echogenicity suggesting a small stone. Inpatient, the patient was given haloperidol, risperidone, and lorazepam. Clarithromycin was discontinued leading to decreased psychosis and improved liver function. At one-month follow-up, the patient was asymptomatic. In general, psychosis with antibiotic use is rare. Thus, the Naranjo scale was developed in 1991 to assess causality adverse drug reactions. For our patient, the score was 6.

Conclusions

Antimicrobials rarely cause neuropsychiatric symptoms including psychosis. Psychotic symptoms include delusions, hallucinations, and disorganized behavior. Antibiomania, coined for antibiotic-induced psychosis, is a side effect reported with macrolide, penicillin, fluoroquinolone, cephalosporin and macrolide use. These CNS side effects can be attributed to easy penetration into the CNS due to its lipid solubility allowing the drug to achieve higher concentrations in the brain tissues. The liver excretes the drug due to its powerful oral bioavailability and long elimination half-life. 14-hydroxy clarithromycin is lipid soluble and able to penetrate the CNS. Clarithromycin alters prostaglandin and cortisol metabolism. It also exhibits its effects by using GABA pathways leading to CNS symptoms. Pharmacokinetics determines clarithromycin's effects. One study investigated penicillin susceptibility to cross blood-brain barriers in animal models causing neurotoxicity via inhibiting GABA inhibitory receptor. Excitatory discharges are released leading to seizures. Findings show the structure of the beta-lactam ring determined by the side-chain. Researchers found that the breakage of the side chain ring reduces epileptogenic properties in patients. Penicillin beta-lactam rings are similar to GABA's inhibitory property in neurotransmission by shortening the duration of "focal discharge". Avoiding degradation from the enzyme which alters the structure of penicillin can avoid these neurotoxic effects.

Cryptococcus meningitis and Neurosyphilis in an advanced HIV patient

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Background

Cryptococcal meningitis is one of the known opportunistic infections in patients with HIV and AIDS. Most commonly isolated species are *C. Neoformans* and *C. gattii*. This fungal species has poor outcomes in immunocompromised patient. Here we present the management and complications in a case of *Cryptococcus meningitis* and neurosyphilis in a patient on HARRT therapy.

Methods

Patient is a 37-year-old homosexual male with past medical history of HIV on HAART, CD4 count 89, Kaposi's sarcoma presented to the ED due to syncopal episodes, altered mental status, and left sided facial swelling. CT head showed mild diffuse cerebral involution greater than expected for the patient's age. First lumbar puncture showed RBC 7, WBC 283, Protein 533, Glucose 27 and positive for cryptococcal antigen. Next three lumbar punctures had elevated opening pressures. Fourth lumbar puncture had low opening pressure, and showed persistently high csf cryptococcal titers greater than 2048.

Results

Pt was treated with Liposomal Amphotericin B, flucytocine/ fluconazole. Patient also showed Serum RPR +, quant 1:32, CD4 89, HIV PCR 46,300. Patient also found to have neurosyphilis and was treated with penicillin IV. Patient then developed acute renal failure, thrombocytopenia, and DIC, which were complications of amphotericin B. Patient received temporary dialysis, cryoprecipitate, and platelet transfusions. Fibrinogen levels were trended for progression of treatment of DIC.

Conclusions

In this report we present complications of uncontrolled HIV infection and its operative infections. Despite being on appropriate antifungals, antibiotics, and antivirals patient had a poor outcome. In this case report we will discuss management and complications of *Cryptococcus meningitis* as well as neurosyphilis in a patient on HARRT therapy.

Laryngeal Tuberculosis A Rare Clinical Entity

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Background

Laryngeal tuberculosis is a rare form of tuberculosis with less than 1% of cases reported in the United States. In 2016, United States had a total of 9,287 new cases of tuberculosis. However, laryngeal tuberculosis is a rare form of tuberculosis, of which less than 1% of cases are reported in the United States. The most common symptoms of laryngeal tuberculosis are dysphonia and odynophagia. In this report, we present a case of a 22-year-old female that presented with dysphonia and odynophagia. She was in good health before the onset of her symptoms, and was diagnosed with laryngeal tuberculosis.

Methods

Patient was a 22-year-old female presented with dry cough, sore throat, and hoarseness for 1 week. She denied fevers, chills, night sweats, chest pain, shortness of breath, sick contacts, or travel history. Ear nose and throat (ENT) exam showed slightly enlarged, boggy tonsils, and a mildly enlarged uvula. No exudates or erythema were noted, chest X-ray was performed, which showed a right middle lobe infiltrate. One month later, the patient returned to the clinic with worsening cough and recurrent voice hoarseness for one week. Her symptoms had initially resolved after treatment with Levaquin. Physical exam revealed inspiratory wheezing. Pulmonary was consulted in order to determine the etiology of the patient's symptoms, as complete resolution was not obtained. The quantiferon test was ordered at that time, but the patient left without performing the test. For continued voice hoarseness, and enlarged tonsils. ENT noticed a mass during direct laryngoscopy and a biopsy was performed, which revealed tuberculosis of the larynxes.

Results

In the United States, laryngeal tuberculosis is not commonly a differential diagnosis for voice hoarseness and is frequently confused with malignancy. Laryngeal tuberculosis is the second most common extrapulmonary manifestation of tuberculosis. Some sources believe that the posterior part of the larynx is most frequently affected due to the recumbent position that allows for pooling of sputum in the posterior larynx. Other sources state that the anterior part of the larynx is twice as often involved compared to the posterior. However, most sources agree that laryngeal tuberculosis most commonly affects the true vocal cords, followed by the false cords, epiglottis, aryepiglottic folds, and the subglottis. The larynx can be involved either via direct spread from the lungs, or by haematogenous spread from parts of the body other than the lungs

Conclusions

In developed countries like the United States, laryngeal tuberculosis is not common. As it is a rare disease, it is very difficult to diagnose and treat an early infection of laryngeal tuberculosis. However, it is important to consider it as part of the differential diagnosis for patients who present with persistent hoarseness of voice that does not resolve despite adequate treatment. If diagnosed early, spread of the infection would decrease and it can have beneficial effects on the patient's health and for all other personal the patient encounters, whom are at risk of getting the infection.

Activity of meropenem-vaborbactam and single-agent comparators against Enterobacterales isolates, including KPC-producing isolates, from European patients hospitalized with pneumonia (2014-2018)

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Background

Meropenem-vaborbactam (MVB) was recently approved in Europe for the treatment of complicated UTIs, including acute pyelonephritis, complicated intra-abdominal infections (cIAI), hospital-acquired bacterial pneumonia (HABP), ventilator-associated pneumonia (VABP), and bacteremia. KPC-producing Enterobacterales (ENT) isolates have disseminated worldwide and are considered endemic in various countries and several hospitals. We evaluated the activity of MVB and single-agent comparators against 5,648 ENT isolates from patients hospitalised with pneumonia (PHP) in European hospitals from 2014–2018.

Methods

Among 5,648 ENT clinical isolates from PHP collected in 40 European hospitals located in 20 countries that were susceptibility (S) tested using reference broth microdilution methods. Of the carbapenem-resistant isolates submitted to whole genome sequencing, 59 carried blaKPC. ENT isolates were also characterized for an extended spectrum beta-lactamase (ESBL) phenotype as described (CLSI, 2019). EUCAST (2019) interpretive criteria were used. %S from intensive care unit (ICU) and non-ICU isolates were also analysed.

Results

The most common ENT pathogens isolated from PHP were *Klebsiella pneumoniae* (KPN; n=1,539) and *Escherichia coli* (EC; n=1,344). Overall, 98.2% of ENT were S to MVB. For 2,663 ENT isolates from ICU patients, MVB %S was 97.5% and for 2,187 non-ICU isolates MVB %S was 98.6%. The %S of comparators for ICU vs non-ICU isolates were similar, except for levofloxacin (76.3%S ICU/ 70.1%S non-ICU). A total of 59 KPC-producing isolates were distributed as follows: 21 isolates were from ICU patients and 38 from non-ICU. KPC-producing isolates were mainly KPN (n=55) and included 44 blaKPC-3, 14 blaKPC-2 and 1 blaKPC-12 from 6 countries. 4 EC contained blaKPC-3. Italy had the highest number of KPC-producing isolates at 38 (64%). MVB inhibited 100% of the 59 KPC-producing isolates. Against isolates with an ESBL-phenotype, MVB inhibited 91.4%. Amikacin was the most active comparator against all ENT (94.3%S); colistin was the most active comparator against KPC-producing isolates (79.7%S).

Conclusions

These results demonstrate MVB has potent activity against ENT isolates from PHP including those producing KPC enzymes and suggest MVB is a useful treatment option for ICU and non-ICU PHP.

Minocycline Activity against *Stenotrophomonas maltophilia* isolated from Patients in US Hospitals

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Background

Stenotrophomonas maltophilia (SM) has emerged as a common hospital-associated opportunistic pathogen found in immunocompromised and immunocompetent patients. SM is intrinsically resistant to many common drug classes, including carbapenems, cephalosporins, and aminoglycosides. Only 4 antibiotics have CLSI breakpoints for SM: minocycline (MIN), ceftazidime (CAZ), levofloxacin (LVX) and trimethoprim-sulfamethoxazole (TMP-SMX). Minocycline is frequently used to treat SM infections. In this study, we analyzed susceptibilities of SM isolates collected as part of the SENTRY Program. We also examined the frequency of SM isolation from pneumonia in hospitalized patients (PIHP) among all Gram-negative (GN) species.

Methods

From 2014-2018, 990 SM isolates were collected from hospitalized patients in 32 US hospitals. Hospitals submitted 1 isolate per patient per infection episode that met local criteria for being the likely causative pathogen and submitted consecutive isolates from pneumonia. Isolates were tested for MIN susceptibility (S) using the CLSI broth microdilution method at JMI Laboratories. Other antimicrobials tested were CAZ, LVX, and TMP-SMX. TMP-SMX was tested 3 of 5 years. All infection types were included in the susceptibility analysis. The prevalence of SM isolates in PIHP during this period was also analyzed.

Results

There were 9,120 GN pathogens isolated from PIHP. The most commonly isolated species was *P. aeruginosa* (34.7%), followed by *Klebsiella pneumoniae* (12.6%), *Escherichia coli* (10.1%), and SM (7.9%). Among the 990 infections caused by SM, PIHP was the most common at 72.4%, followed by bloodstream infections (14.4%) and skin/skin structure infections (6.9%). The %S and MIC_{50/90} values of the 4 antimicrobials tested against SM are as follows: MIN (n=990), 99.5% and 0.5/2.0; CAZ (n=990), 28.5% and 32/>32; LVX (n=990), 77.8% and 1/>4; TMP-SMX (n=609), 94.7% and ≤0.5/>4.

Conclusions

SM was the fourth most frequent cause of GN PIHP in US medical centers. MIN was the most active drug tested against SM with 99.5%S, followed by TMP-SMX (94.7%), and CAZ was the least active with 28.5%S. This study suggests that MIN may be a consideration as a treatment for infections caused by SM, with a very low resistance rate based on CLSI breakpoints.

Delafloxacin Activity against Drug-Resistant *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, and *Moraxella catarrhalis* from US Medical Centers (2014-2018)

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Background

Delafloxacin (DLX) is an anionic fluoroquinolone (FQ) antimicrobial that was approved in 2017 by the United States (US) Food and Drug Administration for the treatment of acute bacterial skin and skin structure infections. DLX recently successfully completed a clinical trial for treatment of community-acquired bacterial pneumonia (CABP). In the present study, in vitro susceptibility (S) results for DLX and comparator agents were determined for CABP pathogens including *Streptococcus pneumoniae* (SPN), *Haemophilus influenzae* (HI), *H. parainfluenzae* (HP) and *Moraxella catarrhalis* (MC) clinical isolates from US hospitals participating in the SENTRY Program during 2014-2018.

Methods

A total of 1,975 SPN, 1,128 HI, 684 MC, and 43 HP isolates were collected from community-acquired respiratory tract infections (CARTI) during 2014-2018 from US hospitals. Sites included only 1 isolate/patient/infection episode. Isolate identifications were confirmed at JMI Laboratories. Susceptibility testing was performed according to CLSI broth microdilution methodology, and CLSI (2019) breakpoints were applied where applicable. Other antimicrobials tested included levofloxacin (LEV) and moxifloxacin (MOX; not tested in 2015). Multidrug-resistant (MDR) SPN isolates were categorized as being nonsusceptible (NS) to amoxicillin-clavulanate, erythromycin, and tetracycline; other SPN phenotypes were LEV-NS or penicillin (PEN)-NS. β -lactamase (BL) presence was determined for HI, HP, and MC.

Results

The activities of the 3 FQs are compared. The most active agent against SPN was DLX, with the lowest MIC_{50/90} values of 0.015/0.03 mg/L. DLX activities were similar when tested against the MDR or PEN-NS for SPN phenotypes. LEV-NS isolates had DLX MIC_{50/90} results of 0.12/0.25 mg/L. DLX was the most active FQ against HI, HP, and MC. BL presence did not affect FQ MIC values for HI or MC; only 2 HP isolates were BL-positive.

Conclusions

DLX demonstrated potent in vitro antibacterial activity against SPN, HI, HP, and MC. DLX was active against MDR SPN that were NS to the agents commonly used as treatments for CABP. DLX had excellent activity against LEV-NS SPN. These data support the continued study of DLX as a potential treatment for CABP.

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Multidisciplinary B-Lactam Allergy Task Force: De-Labeling B-Lactam Allergies One Patient at a Time

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Background

Beta-lactams (BL) are first-line agents for most infections in acute care. Patients labeled as penicillin allergic (PLPA) in the electronic medical record (EMR) frequently receive second-line agents. Nevertheless, most PLPA can safely receive a cephalosporin (Cp). Published protocols focus on de-labeling the penicillin allergy and include penicillin skin testing. We sought to evaluate the ability of history alone (i.e., EMR review and interview) to identify PLPA who can safely receive a Cp.

Methods

We prospectively identified patients 18 years or older at a tertiary care academic hospital, from 2/13/19 through 4/19/19, who received aztreonam, clindamycin, fluoroquinolones, meropenem. Among these, patients were included with a label of penicillin allergy without concurrent allergy to other BL. The authors (antimicrobial stewardship pharmacist, internal medicine resident/pharmacist and infectious disease physician) interviewed the patients and reviewed the EMR. In addition, the authors included all PLPA encountered in their practice, regardless of current antibiotics. Tolerance to a penicillin was considered proof of tolerance to all Cps. Tolerance to a Cp was considered proof of tolerance to its generation or higher, except for cefazolin, which was considered only proof of tolerance to itself due to its unique side chain. The primary outcome was the number of patients identified as tolerant to Cps without additional testing. Allergy profiles of all patients tolerant of BL were updated and a dedicated allergy assessment note was placed in the patient's EMR.

Results

A total of 45 patients were identified; 5 were excluded due to unobtainable history. We found no patients with absolute contraindication to Cps (i.e., type II-IV hypersensitivity reaction). Thirty-one patients out of 40 (77.5%) had EMR-documented administration of a penicillin or Cp without adverse reaction. The lower generation BL tolerated was: ampicillin (1), piperacillin (2), cephalexin (10), cefazolin (6), cefuroxime (5), ceftriaxone (5) and cefepime (2). Interview identified 3 additional patients tolerant to amoxicillin and 1 to cephalexin.

Conclusions

In our institution, 87.5% of patients labeled as penicillin allergic were identified as safe to receive a Cp, the majority per EMR review.

Healthcare Burden and Costs of Recurrent *Clostridioides difficile* Infection in the Medicare Population

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Background

Clostridioides difficile infection (CDI), especially recurrent CDI (rCDI), is associated with high morbidity and healthcare resource utilization (HRU), imposing significant burden on older adults. This study evaluated HRU and all-cause, direct medical costs in CDI patients with and without rCDI in the Medicare population.

Methods

Retrospective analysis of claims data from the 100% Fee-for-Service Medicare database was performed. Patients with an index CDI episode requiring inpatient stay (diagnosis codes: ICD-9 008.45; ICD-10 A04.7, A04.71, or A04.72) or an outpatient CDI visit with CDI treatment were identified between January 2010 and December 2016. Patients included were those continually enrolled in Medicare Part A, B, and D for 12 months before and 12 months after the first date of the index CDI episode. Each CDI episode was followed by a 14-day period with no CDI claims after the end of treatment to distinguish rCDI from index episode CDI. rCDI was defined as another CDI episode within an 8-week window immediately after the claim-free period. HRU and costs were captured for 12 months of follow-up, stratified by increasing number of rCDI episodes.

Results

268,762 patients had an index CDI episode. Mean (SD) age was 78.3 (8.0) yrs, 69.0% were female. 175,554 (65.3%) had no rCDI, 38,163 (14.2%) had 1 rCDI, 22,898 (8.5%) had 2 rCDI, and 32,147 (12.0%) had 3+ rCDI in the 12-month post-index period. During the 12-month follow-up, 85% of patients had at least 1 hospitalization and a substantial number of patients had ≥ 3 hospitalizations (no rCDI: 23.8%, 1 rCDI: 34.0%, 2 rCDI: 37.4%, and 3+ rCDI: 40.9%). Mean (SD) length of hospital stay was 13.4 (17.2) days and approximately 18 (20) days for those without and with rCDI, respectively. Total, all-cause, direct medical costs per patient during follow-up, by increasing number of rCDI episodes, were \$76,024, \$99,348, \$96,148, and \$96,517, with 53% to 60% driven by inpatient and post-acute care costs.

Conclusions

More patients with recurrent CDI had repeat hospitalizations than those with no recurrence, and a longer duration of hospital stay. All-cause, direct medical costs were also substantial and higher in these patients. Reduction of recurrences is warranted to reduce the overall burden of CDI.

Therapeutic Drug Monitoring (TDM) of β -Lactams in Extended-Spectrum β -Lactamase (ESBL)-Producing Enterobacterales Bloodstream Infections

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Background

Available literature in β -lactam therapeutic drug monitoring (TDM) support targeting 100% fT >4xMIC (fCmin:MIC >4) in critically ill patients to maximize bactericidal activity and optimize clinical outcomes. There is currently a gap in data for utilization of β -lactam monitoring to optimize pharmacokinetic and pharmacodynamic (PK/PD) targets in multidrug resistant pathogens. The objectives of this study were to analyze attainment of PK/PD targets with β -lactams and to further assess patient outcomes in hospitalized patients with extended-spectrum β -lactamase (ESBL)-producing Enterobacterales bloodstream infections.

Methods

This study was a single center, retrospective chart review conducted from July 2016 to 2019 in adults who received TDM for meropenem, cefepime, or piperacillin for treatment of an ESBL bloodstream infection. Patients being treated for a polymicrobial bacteremia were excluded. Total plasma concentrations were obtained at steady-state and adjusted for protein binding to estimate unbound drug. The primary outcome was attainment of fCmin:MIC ≥ 4 . Secondary outcomes included in-hospital mortality, microbiologic cure, and clinical cure. Microbiologic cure was defined as presence of negative blood cultures during the index hospitalization, without subsequent positive blood cultures. Clinical cure was defined as complete resolution of all signs and symptoms caused by the infection and no additional antibiotic therapy required.

Results

Fifteen patients were included in the study. Eight meropenem, 6 cefepime, and 1 piperacillin concentrations were assessed. The mean total daily doses used were meropenem 4.4g, cefepime 4.5g, and piperacillin/tazobactam 13.5g. Fourteen (93.3%) patients received intermittent infusions. Thirteen (86.7%) patients achieved fCmin:MIC ≥ 4 . Ten of those patients achieved fCmin:MIC ≥ 10 . The dose was decreased in 50% (n=5) of patients that had a fCmin:MIC ≥ 10 . The mortality rate of this cohort was 6.7% (n=1). One patient (6.7%) experienced microbiologic failure and five patients (33.3%) experienced clinical failure despite achieving fCmin:MIC ≥ 4 . No adverse drug reactions were observed in this cohort.

Conclusions

The majority of patients in this cohort achieved the PK/PD target fCmin:MIC ≥ 4 . This target provided a microbiologic cure rate of 93% in ESBL bacteremic patients. A third of the patients had fCmin:MIC ≥ 10 requiring dosage adjustment. TDM of beta-lactams ensures safe, effective therapy in patients with MDR infections.

Variation among infectious diseases pharmacists for the treatment of *Staphylococcus aureus* bloodstream infections

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Background

Staphylococcus aureus bloodstream infections (SABSI) are a complex infection. Optimal treatment for patients with SABSI, in particular those with complicated or persistent infection, remains unclear. Two recent surveys have demonstrated practice variations in SABSI among infectious diseases (ID) physicians. The purpose of this survey was to examine practice variations in SABSI among ID pharmacists.

Methods

A multiple-choice survey was electronically distributed to ID pharmacist members of the American College of Clinical Pharmacy (ACCP) Infectious Diseases Practice and Research Network (IDPRN) to determine differences in the management of SABSI, as well as the definition and treatment of persistent SABSI. Descriptive statistics were calculated to characterize participants' demographic and practice characteristics, in addition to diagnostic and treatment strategies. Data were analyzed utilizing Pearson's Chi-Square or Fisher's Exact Test, as appropriate. A 2-sided P value of 0.05 was considered statistically significant. Statistical analyses were performed using SPSS (version 24.0, IBM, Armonk, New York).

Results

A total of 130 ID pharmacists responded to the survey. Anti-staphylococcal penicillins were preferred for MSSA blood stream infections (BSI) in patients with central nervous system infection and infective endocarditis whereas cefazolin was favored for most MSSA BSI patients. Definition of persistent SABSI varied with 50% classifying persistent SABSI as at least 4 to 6 days of positive blood cultures. Respondents reported a variety of treatment strategies for persistent SABSI, of which 34% selected daptomycin alone while 38% elected to combine daptomycin and ceftaroline. Hospital size was associated with treatment choice for persistent MRSA BSI. Pharmacists at hospitals less than 500 beds were more likely to use daptomycin, while those at hospitals greater than 500 beds were more likely to use daptomycin and ceftaroline ($p < 0.05$). Only 31.1% of pharmacists practiced at hospitals with mandatory ID consultation for SABSI. A majority (67.7%) had rapid diagnostics for identifying SABSI, but 26% of those facilities with rapid diagnostic technology did not notify pharmacy of the results.

Conclusions

A survey of ID pharmacists showed variation in the management of SABSI, as well as the definition and treatment of persistent SABSI. Mandatory ID consultation has not been widely implemented, and rapid diagnostic technology has not been fully adopted or optimized. Treatment choices for persistent MRSA BSI were associated with hospital size.

Evaluation of Oxacillin-Susceptible, Methicillin-Resistant Staphylococcus aureus (OS-MRSA) at a Community Hospital

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Background

Beta-lactam resistance in methicillin-resistant staphylococcus aureus (MRSA) is determined by the presence of the *mecA* gene, which encodes a modified penicillin-binding protein (PBP2a) that has poor affinity for nearly all beta-lactam antibiotics. MRSA may express heterogeneous resistance to beta-lactams, meaning that all cells in the culture carry the genetic information for resistance but only a subpopulation express the resistance, making the detection of oxacillin resistance difficult. The purpose of this study is to investigate the prevalence and epidemiology of oxacillin-susceptible, *mecA* positive, *S. aureus* (OS-MRSA) at a community hospital.

Methods

In this retrospective, single-center, observational study, microbiology reports from January 2011 to June 2019 were reviewed to identify patients with infections caused by MRSA. Adult patients with a positive MRSA culture collected in the emergency department or during admission were included. Antimicrobial susceptibility testing was performed per the Clinical Laboratory Standards Institute (CLSI) guidelines. The primary outcome measure was the percentage of patients with OS-MRSA, as defined by an oxacillin MIC \leq 2 mg/L with a positive cefoxitin screen, compared to MRSA. To assess clinical features and secondary outcomes between the groups, a randomized MRSA sub-group was identified.

Results

A total of 1597 unique MRSA culture were identified and met inclusion criteria. Among the 1597 MRSA cultures, 1313 individual patient encounters and 1005 unique patients were identified. The incidence of OS-MRSA was 2.99% (30/1005). Baseline characteristics were similar between the groups. The average hospital length of stay for the OS-MRSA group (12.6 ± 8.8 days) was not statistically different as compared with the MRSA subgroup (14.4 ± 9.8 days) ($p=0.468$). The average total days of antibiotic therapy were higher for the MRSA sub-group (39.8 ± 26.8) as compared to the OS-MRSA group (30.6 ± 31.0 days) ($p=0.219$). All-cause 30-day mortality was higher in the MRSA sub-group when compared to the OS-MRSA group (27% vs. 15% respectively, $p= 0.362$).

Conclusions

To the best of our knowledge, the findings described in this study represent the first epidemiological description of OS-MRSA in a community hospital. OS-MRSA was identified in both community and hospital infections. Patients infected with MRSA did not have higher rates of 30-day mortality compared with patients with OS-MRSA. The results of this study demonstrate the clinical importance of testing *S. aureus* isolates for the *mecA* gene. However, given the small sample size, additional studies are warranted to validate this data.

Comparison of alternative vancomycin dosing methods using area under the curve based monitoring in obese patients

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Background

Dosing vancomycin in obese patients can be particularly challenging. Current guidelines recommend vancomycin doses of 15-20 mg/kg targeting trough levels of 10-20 mcg/mL. A recent study found that allometrically-scaled vancomycin dosing was superior to guideline-based dosing for achieving initial trough levels within the target range, especially in patients with body mass index ≥ 30 kg/m². Allometry is the study of the relationship between physiology and body size to scale drug doses between species. Allometric scaling results in smaller mg/kg doses in obese patients, reducing overexposure to vancomycin yet maintaining therapeutic levels. Many studies have shown the benefits of area under the curve (AUC)-based vancomycin monitoring, including less vancomycin-associated nephrotoxicity. Treatment success against *Staphylococcus aureus* has been seen with AUC to MIC ratios ≥ 400 mcg*H/mL, while AUC to MIC ratios >650 mcg*H/mL has been linked to nephrotoxicity. This study aims to compare attainment of AUCs of 400-600 mcg*H/mL when using various vancomycin dosing methods in obese patients.

Methods

Patients admitted between October 2018 and June 2019 who received allometrically dosed vancomycin were reviewed. The study included patients ≥ 19 years old, BMI >30 kg/m², and with a calculated steady-state AUC. Patients were excluded if they received vancomycin as prophylaxis, had severe renal dysfunction, pregnancy, malignancy, or cystic fibrosis. Patient-specific AUCs were calculated using the trapezoidal rule and two steady-state, post-infusion vancomycin levels. A predicted AUC using patient-specific vancomycin clearance was calculated for the following alternative dosing methods: allometric, corrected body weight (CBW) using 15 mg/kg, and 12.5 mg/kg total body weight (TBW). Each was compared to a predicted AUC calculated using consensus 15 mg/kg TBW dosing. The primary outcome was attainment of initial AUC within the target range of 400-600mcg*H/mL for each dosing method.

Results

A total of 223 patients were reviewed, 84 of which met inclusion criteria. Initial AUC between 400-600 mcg*H/mL was achieved in 63% of CBW doses, 57% for both allometric and 12.5 mg/kg TBW, and 37% for 15 mg/kg TBW. All alternative dosing methods were statistically significant compared to guideline-based dosing ($p < 0.05$). The average AUC for each dosing method was as follows: 480 mcg*H/mL for CBW, 557 mcg*H/mL for allometric, 546 mcg*H/mL for 12.5 mg/kg, and 653 mcg*H/mL for 15 mg/kg ($p < 0.05$).

Conclusions

Alternative dosing methods of vancomycin were significantly more likely to achieve initial AUC within range vs. conventional 15 mg/kg doses in the obese population. Further studies are needed to optimize the dosing of vancomycin in obese patients.

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Local Validation of *Pseudomonas aeruginosa* Risk Factors: Results and Implication for Decision Support Tools

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Background

Pseudomonas aeruginosa (PSA) is a serious public health threat, causing an array of infections including pneumonia (PNA). Often these infections are hospital-associated and categorized as multidrug-resistant (MDR), resulting in overuse of empiric broad-spectrum antibiotics. This evaluation was conducted to obtain local validation results for PSA infections in the fiscal year 2018 (FY18).

Methods

Positive PSA culture reports in FY18 were obtained from microbiology. A retrospective review of patient electronic health records was conducted with collection of: PSA cases were treated or not (non-pathogenic), illness severity (critically ill or not), 6 MDR risk factors, susceptibilities, and source of culture. Patients were categorized into four groups based on illness severity and if the PSA was treated or not.

Results

The FY18 evaluation resulted in identification of 89 positive PSA cases involving 78 patients in 47 unique hospitalizations; 46 (52%) cases received PSA treatment. Of 46 treated cases, representing 29 of 5145 (0.6%) hospitalizations, 17 cases (37%) involved critically ill patients (16 (0.3%) hospitalizations). Prevalence of 6 MDR risk factors among patients receiving PSA treatment were (% critically ill vs. % not-critically ill cases): admission from nursing home/assisted living (18% vs. 3%), history of PSA culture in last 12 months (18% vs. 14%), immunosuppressant use in last 30 days (24% vs. 14%), history of transplant (6% vs. 7%), hospitalization in last 90 days (65% vs. 45%), antibiotic use in last 90 days (76% vs. 55%). Of critically ill, treated cases (n=17), 2 isolates were non-susceptible to piperacillin/tazobactam, and 1 to cefepime. Seven cases of MDR PSA were identified; 5 were non-pathogenic, while 0 and 2 cases were treated in critically ill and non-critically ill patients, respectively. Over FY18, 2.6% of inpatients with a diagnosis of PNA (10 of 381 cases) tested positive for PSA lung infection, 8 of which were in critically ill patients.

Conclusions

Infection with PSA was rare in FY18 (<1% of total admissions). Generally, MDR risk factors were more prevalent in critically ill patients. Resistant PSA infections were rare in critically ill patients, suggesting empiric PSA double-coverage may not be necessary. MDR PSA infection was uncommon; most of MDR PSA were non-pathogenic. Non-critically ill patients with PSA PNA were rare (<1%), suggesting empiric PSA coverage may not be necessary for suspected PNA of non-critical illness. The result of the local validation of PSA risk factors will inform revisions to decision support tools for disease states such as PNA as a local, population-based approach.