2019 ASHP Midyear Clinical Meeting Roundtable/Poster Session Summary: Pediatrics

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Acid Suppression for Stress Ulcer Prophylaxis in Pediatric Patients Within a Pediatric Intensive Care Unit

Leigha Davis, PharmD[1]; Andrew Allison, PharmD, BCPPS[1];
Margaret Mathewson, MD[2]; Micah Butcher, PharmD, BCPPS[1]
Department of Pharmaceutical Services[1]; WVU School of Medicine[2], Morgantown, West Virginia

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Background

- Proton pump inhibitors (PPIs) and histamine-2 receptor blockers (H2RAs) are commonly used within pediatric intensive care units (PICU) to minimize the risk of stress ulcer-related gastrointestinal bleeding.
- There is limited data to guide assessment of risk for stress-related GI bleed or for appropriate indications for the use of stress ulcer prophylaxis (SUP) in the PICU.
- Inappropriate use of acid suppression agents can increase incidence of adverse effects, such as hospital-acquired pneumonia, hospital-acquired *Clostridioides difficile* infection, and increased risk of bone fractures.
- Additionally, this therapy is sometimes continued at time of transfer to floor units or by prescription to home at discharge.

Objectives

- **Primary:**
  - To characterize the documented indications and risk factors for use of acid suppression agents in pediatric patients within the PICU
- **Secondary:**
  - To identify the percentage of use of acid suppression agents without documented indications or risk factors
  - To identify the incidence of continuation of acid suppression agents upon transfer to floor units or at discharge
  - To describe the acid suppression regimens used in the PICU

Methods

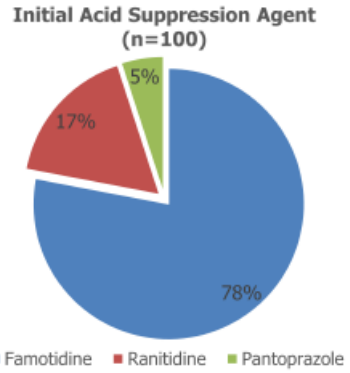
- This IRB-approved retrospective chart review of pediatric patients characterized acid suppression therapy use in the PICU.
- Patients were excluded if they received a PPI and/or H2RA at home prior to admission.
- Data collected included: demographics, acid suppression agents and classes initiated, dose and route, duration of therapy, incidence of dual class therapy, risk factors present within 24 hours prior to initiation, and whether therapy was continued at PICU/ hospital discharge.
- Objectives were analyzed using descriptive statistics.

Results

Demographics	(n=100)
Age, median, years (range)	3 (0 – 18)
Male, %	53

Results

Select Risk Factors Present Within 24 hours Prior to Acid Suppression Therapy	(n=100)
Enteral nutrition ≤ 50% of goal rate/day	90%
Parenteral nutrition / nothing by mouth (NPO) status	75%
Mechanical ventilation	32%
NSAID use	29%
High dose steroid use (≥ 50 mg/m²/day (≥ 30 mg/m²/day in neonates) of hydrocortisone or equivalent)	28%
Shock (use of vasopressors)	20%
Neurologic failure (GCS ≤ 11)	19%
Respiratory failure (peak inspiratory pressure > 25 cm H_2O)	17%
Anticoagulant use	10%
No identifiable risk factors	5%



Dosing of Therapy	
Flat dosing	22%
Famotidine	20 mg twice daily
Weight-based dosing (mg/kg/day)	78%
Famotidine dose, mean	0.72
Ranitidine dose, mean	3.68
Pantoprazole dose, mean	1

Results

Characterization of Therapy	(n=100)
Initial Acid Suppression	
Intravenous route	66%
Duration of Use	
Acid suppression therapy, median	4 days (1 – 525)
H2RA therapy, median (n = 97)	4 days (1 – 525)
PPI therapy, median (n =12)	4.5 days (1 – 46)
Dual Class Therapy	
Incidence of dual class therapy	8%
Duration of use, median (n = 8)	2.5 days (1 – 46)
Acid Suppression Therapy Continuation	
At PICU discharge	47%
At hospital discharge	23%

Discussion

- The most common risk factors associated with H2RA/PPI use were enteral feeds at ≤ 50% of goal (90%), NPO status (75%), mechanical ventilation (32%), use of NSAIDS (29%), use of high dose steroids (28%), and use of vasopressors (20%).
- There is no link established between enteral feeding status and the risk of stress ulceration in pediatric literature.
- The results of this medication use review will provide meaningful education to providers in an effort to standardize the prescribing of H2RAs/PPIs for stress ulcer prophylaxis.

Conclusions

- Practices of acid suppression administration were closely linked to enteral feeding status, use of mechanical ventilation, and the concurrent use of certain medication classes.
- Five patients had no identifiable risk factors present in the medical record.
- Nearly one-fourth of patients prescribed new acid suppression therapy were continued on therapy at hospital discharge.
- The most commonly prescribed acid suppression regimen was famotidine 0.5 mg/kg/day.

References

- References available upon request

closure: Authors have no conflicts of interest to disclose.

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Assessing pharmacist adherence with medication management processes in a pediatric academic medical center

Lubna Mazin PharmD, Matt Sapko PharmD, MS, Chet Kaczor PharmD, MBA, Jessica Fischer PharmD, MS
Nationwide Children's Hospital Department of Pharmacy

Background

In 2016, Ohio passed the Consult Agreement Law which expanded pharmacist's scope of practice to allow pharmacist to initiate, modify, and discontinue drug therapy with physicians

Consult agreement rule passed by the Ohio Board of Pharmacy requires a Quality Assurance (QA) program

Consult agreement rule removed pharmacists' ability to modify drug therapy under P&T committee approved procedures

Objectives

- Develop and implement a QA program using a Plan Do Study Act (PDSA) cycle
- Assess adherence with each quality metric within the consult agreement policies and procedures
- Determine the cost of implementing a QA program

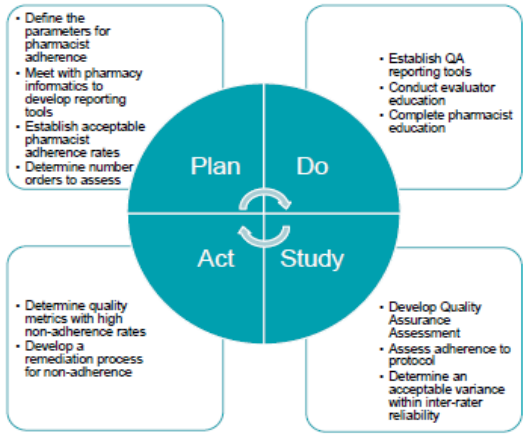
Methods

Adherence is defined as: 90% of pharmacists' actions follow corresponding policies and procedures

QA program team will include the directors of the inpatient and ambulatory pharmacy, pharmacy supervisors, clinical coordinators, clinical pharmacists, staff pharmacists, and pharmacy informatics

Timeline was created to guide the progress of QA program development

Pharmacy informaticists used the electronic health record (EHR) to pull data from the inpatient and outpatient pharmacy patient charts



Results

Figure 1: Nationwide Children's Hospital Institutional Collaborative Practice Agreement (Quality Metrics)

Electronic Health Record Report

- Adjusting medication administration times
- Discontinuation of sucrose
- Dispensing quantity adjustments
- Adjusting doses within 10%
- Modification of dosage forms
- Converting dose frequencies from scheduled to once
- Discontinuation of duplicate saline flush orders
- Initiating carrier fluids
- Dosing of pre-operative antibiotics
- Prescribing medication administration supplies

Simulation and Chart Review

- Medication reconciliation
- Therapeutic drug monitoring

Discussion

Strengths

- Inter-rater reliability assessment
- Pharmacy department collaboration
- PDSA study design
- Aligns with health-system and department of pharmacy strategic plan
- Spans inpatient and outpatient departments of pharmacy

Limitations

- Fragmentation of reporting ability between inpatient and outpatient pharmacy, despite shared EHR
- Resource intensive to run reports and to complete manual chart reviews to audit each quality metric
- Different methods of assessing adherence

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Disclosures

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

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ALeigha Davis, PharmD1; Andrew Allison, PharmD, BCPPS1; Margaret Mathewson, MD2; Micah Butcher, PharmD, BCPPS1
Lubna Mazin PharmD, Matt Sapko PharmD, MS, Chet Kaczor PharmD, MBA, Jessica Fischer PharmD, MS

Bivalirudin for Anticoagulation in Patients on Ventricular Assist Device Support at a Children's Hospital: Percent Time in Therapeutic Range

Christine Boulos PharmD; Joanne Lee PharmD, BCPS, BCPPS; Jenna Murray CPNP; Jeffrey Moss PharmD, BCCCP; Sharon Chen MD, MPH

Departments of Pediatrics (Cardiology) and Pharmacy, Stanford University, Lucile Packard Children's Hospital (LPCH) Stanford, Palo Alto, CA

Introduction

- Children with severe heart failure may require advanced mechanical circulatory support (MCS) with a ventricular assist device (VAD) if medical and surgical options fail.
- Thromboembolic and bleeding complications associated with VAD support are a major cause of morbidity and mortality.[1,3]
- Although heparin has been the standard of care, challenges in achieving stable therapeutic levels and adverse events have led to increasing use of bivalirudin as an alternative anticoagulant.[3-7]
- Available literature suggests bivalirudin may be safely used in the pediatric population but there is limited evidence regarding its use for VAD anticoagulation.[2,4,5]

Objectives

The aim of this study was to determine the percent time in therapeutic range (%TTR) while on bivalirudin in pediatric VAD patients at a single center cardiac program.

Methods

- This was a **retrospective chart review** of pediatric VAD patients admitted to LPCH between January 2014 to November 2019.
- **Inclusion criteria**: paracorporeal VAD support, bivalirudin as the primary agent for VAD anticoagulation
- **Exclusion criteria**: intracorporeal VAD support, heparin as the primary agent for VAD anticoagulation, bivalirudin used for pump thrombosis
- The **primary endpoint** was %TTR while on a continuous bivalirudin infusion. Therapeutic range was defined as a patient-specific activated partial thromboplastin time (aPTT) range that varied over time as determined by a clinical team with expertise in MCS.
  - aPTT levels were collected from time of bivalirudin initiation until discontinuation due to either transition to another anticoagulant, heart transplant, or death.
  - Extrapolation of the Rosendaal linear interpolation method was used for calculation of %TTR.
- **Secondary endpoints** included time to first goal aPTT range and average bivalirudin dose at aPTT target range of 70 to 90 seconds.

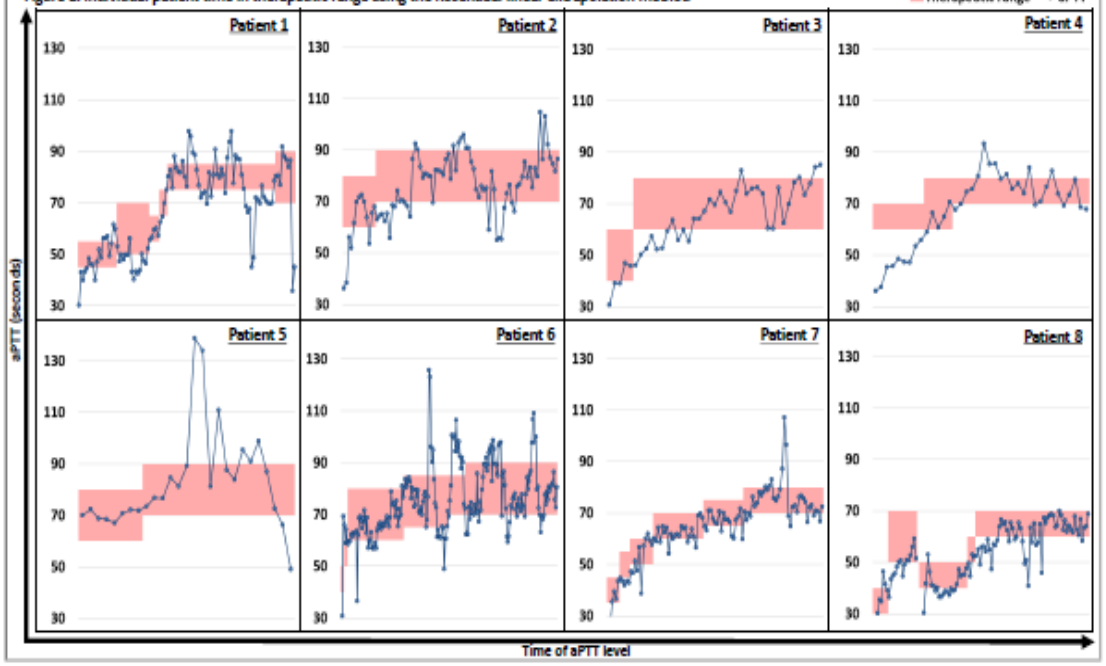
Results

Table 1. Characteristics of pediatric VAD patients on bivalirudin for anticoagulation

Patient	Age (months)	Weight (kg)	Underlying diagnosis	VAD (type)	VAD (device)	Initial bival dose (mg/kg/hr)	Max bival dose (mg/kg/hr)
1	3.0	3.9	CM	LVAD	Berlin	0.05	0.95
2	6.0	5.9	CM	LVAD	Berlin	0.10	1.54
3	9.1	7.4	CM	LVAD	Berlin	0.03	1.20
4	63.6	18.8	CHD	LVAD	Berlin	0.20	0.96
5	0.4	4.1	CM	BiVAD	Pedimag	0.20	0.27
6	2.8	4.9	CM	LVAD	Berlin	0.20	1.70
7	16.8	8.8	CHD	SVAD	Berlin, Centrimag	0.05	0.30
8	31.2	11.4	CHD	SVAD	Berlin, Centrimag	0.05	1.04
Median (Range)	7.6 (0.4-63.6)	6.7 (3.9-18.8)	-	-	-	0.08 (0.03-0.20)	1.00 (0.27-1.70)

Abbreviations: bivalirudin (bival), cardiomyopathy (CM), chronic heart disease (CHD), left ventricular assist device (LVAD), biventricular assist device (BiVAD), single ventricular assist device (SVAD)

Figure 1. Individual patient time in therapeutic range using the Rosendaal linear extrapolation method



Results

Table 2. Bivalirudin %TTR and average dose to achieve aPTT range of 70 to 90 seconds

Patient	Days in range	Total days on bival	%TTR	Time to first goal range (hr)	Bival dose at aPTT 70-90 sec (mg/kg/hr), mean (SD)
1	12.6	27.7	45.4	33.6	0.69 (0.16)
2	17.7	27	50.8	40.8	1.01 (0.33)
3	7.7	12	57.4	33.6	0.76 (0.31)
4	4.5	8.9	64.5	48.0	0.65 (0.19)
5	5.1	8.9	65.5	0.0	0.23 (0.05)
6	70.3	94.1	67.8	16.8	1.15 (0.35)
7	20.5	29.8	68.6	12.0	0.36 (0.07)
8	23.9	35.2	74.7	16.8	1.04 (0.00)
Median (Range)	15.2 (4.5-70.3)	27.4 (8.9-94.1)	65.0 (45.4-74.7)	25.2 (0.0-48.0)	0.73 (0.23-1.15)

- Eight patients with a total of 244 patient-days on bivalirudin were included in this study.
- The combined overall time within therapeutic range was 162 days with a median %TTR of 65% (range 45-75%).
- The first therapeutic aPTT level was reached after a median of 25.2 hours (range 0.0-48.0 hours) after initiation of bivalirudin infusion.
- The median bivalirudin dose corresponding with aPTT levels between 70 to 90 seconds was 0.73 mg/kg/hr (range 0.23-1.15 mg/kg/hr).

Conclusions

- Bivalirudin achieves target anticoagulation goals for a majority of therapy duration and can be utilized for pediatric VAD anticoagulation.
- More studies evaluating clinical outcomes are needed to determine the safety and efficacy of bivalirudin for VAD anticoagulation.
- A future comparison of bivalirudin to heparin would be valuable in assessing various anticoagulation strategies in this population.

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Correspondence: Christine Boulos (Cboulos@stanfordchildrens.org)

Bivalirudin for Anticoagulatin in Patients on Ventricular Assist Device Support at a Children's Hospital: Percent Time in Therapeutic Range
Christine Boulos, PharmD; Joanne Lee, PharmD, BCPS, BCPPS; Jenna Murray, CPNP; Jeffrey Moss, PharmD, BCCP; Sharon Chen, MD, MPH

Evaluating the use of heparin derivatives in overweight and obese pediatric patients: a review

Michael P. Garner, PharmD Candidate; Chimnonso P. Onuoha, PharmD Candidate;
Norman E. Fenn III, PharmD, BCPS
University of Texas at Tyler - Fisch College of Pharmacy

BACKGROUND

- According to the CDC, one in five minors in the United States are described as obese.[1]
- Obese children are at higher risk of a hypercoagulable event, such as venous thromboembolism, compared to healthy weight children.[2]
- Concerns exist with the narrow therapeutic window of anticoagulants in general, and especially with children.[3]
- The use of low molecular weight heparins (LMWHs) in anticoagulation prophylaxis in overweight and obese children has been sparsely studied.

OBJECTIVES

- Evaluate and describe current available literature on the use of heparin derivatives in overweight and obese pediatric patients
- Assess efficacy and safety parameters of heparin derivatives in overweight and obese pediatric patients

METHODS

- A comprehensive literature search of PubMed, SCOPUS, Cumulative Index of Nursing and Allied Health, Academic Search Complete, PsycInfo, Cochrane Library, and Web of Science databases was conducted.
- Search terms used were "LMWH OR low molecular weight heparin OR enoxaparin OR dalteparin OR tinzaparin OR fondaparinux," AND "pediatric OR child OR children," AND "obese OR obesity OR overweight."
- No limits or timeline restrictions were imposed.
- Studies were included if they contained pediatric patients who were overweight or obese and received either enoxaparin, dalteparin, tinzaparin, or fondaparinux.
- Exclusion criteria: Duplicate studies; off-topic studies; adult studies; inaccessible full articles; non-English studies; animal trials.

RESULTS

Figure 1: Number of evaluated studies retrieved

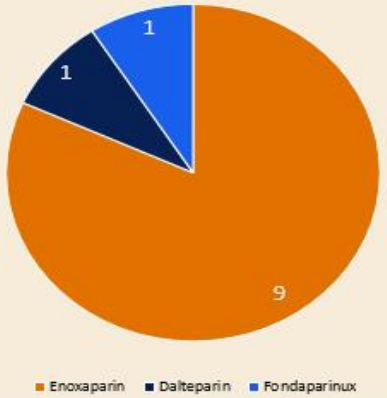


Figure 2: Changes in enoxaparin doses to reach therapeutic anti-factor Xa measurements

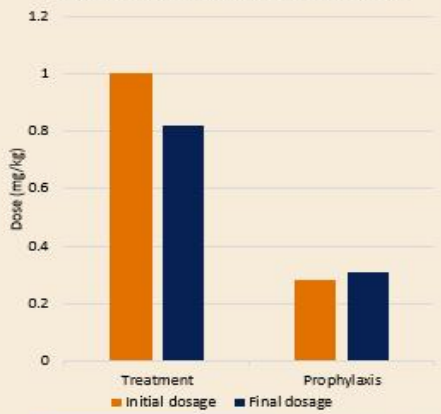
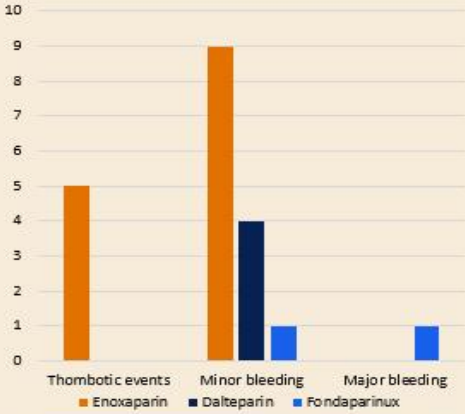


Figure 3: Number of safety events



RESULTS

- Enoxaparin was the most studied heparin derivative in obese pediatric patients.
- Evidence for dalteparin and fondaparinux were limited; no studies using tinzaparin in this population were retrieved.
- Enoxaparin dose reductions of 13% to 37% occurred from baseline within the treatment studies.
- Prophylactic dose increases of enoxaparin from baseline ranged from 0% to 27.3%.
- Monitoring of anti-factor Xa measurements was inconsistently performed or reported by investigators.
- Fourteen minor bleeding events were reported in the literature along with one major bleeding event.
- Three thrombus extensions and two new thrombotic formations were described.

DISCUSSION

- The observed decrease seen from the enoxaparin treatment studies suggests that obese pediatric patients may be receiving supratherapeutic dosing initially.
- Prophylactic doses of enoxaparin were unchanged in two of three studies regardless of monitoring due to study protocol.
- Minor bleeding events were the most commonly reported safety parameter, with only one incidence of a major bleed inferred in the literature.
- The observed lack of monitoring is concerning due to the narrow therapeutic window of these agents, potentially placing patients at greater risk for safety concerns.
- Presently, there is no sub-stratification of obesity in pediatric patients, which could have a dramatic influence on future dosing of heparin derivatives.

CONCLUSIONS

- Enoxaparin is the most frequently described anticoagulant in the obese pediatric literature.
- Monitoring should be performed using anti-factor Xa measurements, although controversy does exist with the use of these measurements.
- Larger, long-term randomized controlled trials are needed to determine optimized treatment strategies on the heparin derivatives for better clinical outcomes in the overweight or obese pediatric population.

REFERENCES

For the full list of references, abstract, and more information use this QR code

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Michael P. Garner, PharmD Candidate; Chimnonso P. Onuoha, PharmD Candidate; Norman E. Fenn III, PharmD, BCPS

Evaluation of Atypical Antipsychotics for Treatment of Delirium in the Pediatric Intensive Care Unit (PICU)

Brianna Henson, PharmD[1]; John Donnelly, PharmD[1]; Mary Subramanian, PharmD, BCPS, BCPPS[1]; Lauren Wyatt, PharmD[1]
[1]Wake Forest Baptist Health Brenner Children's Hospital

Acknowledgement: Joseph Rigdon, PhD for statistics

Brenner Children's
WAKE FOREST BAPTIST HEALTH

Background

- Delirium may occur in up to 29% of critically ill pediatric patients[1]
  - Limited data for treating hyperactive delirium with antipsychotics in this population
    - Trial by Joyce and colleagues resulted in no significant adverse effects using quetiapine in 50 patients[2]
    - Sassano-Higgins and colleagues evaluated olanzapine in 31 patients and showed a reduction in delirium symptom severity[3]
- Brenner Children's Hospital (BCH) PICU management of delirium

Prevention	Identification	Non-pharmacologic	Pharmacologic
- Treat underlying condition - Treat withdrawal and pain - Limit medications that may contribute - Benzodiazepines - Anticholinergics - Narcotics	- Cornell Assessment of Pediatric Delirium (CAPD) screen every 12 hours if State Behavioral Scale (SBS) ≥ -1 - CAPD ≥ 9 indicates delirium	- Early mobilization - Cognitive stimulation - Clustered care -Sleep hygiene	- Alternative sedatives - Remove delirium inducing medications - Antipsychotics for refractory agitation

- Recent systematic review in 5,667 adult ICU patients with delirium[4]
  - No improvement in patient outcomes associated with antipsychotic use
  - Potentially harmful cardiac effects

Purpose

- To evaluate the effect of atypical antipsychotics on CAPD scores in pediatric patients with hyperactive delirium

Objectives

- Primary
  - Difference in CAPD scores 3 days prior compared to 3 days after initiation of antipsychotic (day 4 = first day of treatment)
- Secondary
  - Duration of antipsychotic treatment
  - Concomitant opioid and benzodiazepine use
  - Other confounding factors for delirium
  - QTc interval following antipsychotic initiation

Methods

- Study Design
  - Single-center, retrospective chart review conducted in the BCH PICU
- Study Population
  - Inclusion
    - Patients admitted to the BCH PICU from 4/1/2018 to 10/24/2019
    - Received aripiprazole, olanzapine, quetiapine, or risperidone ≥ 3 days
  - Exclusion
    - < 3 days of treatment
    - No documented CAPD scores
    - Antipsychotic resumed from home
    - Indication other than delirium

Results

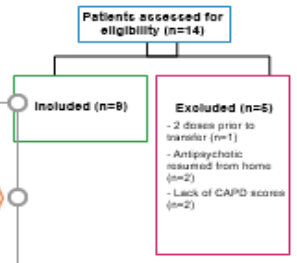


Table 1: Baseline and Treatment Characteristics

Age in years, median (Range)	7 (0.52-15)
Weight in kg, median (Range)	20.3 (5.9-81.8)
Developmental delay, n (%)	4 (44%)
Antipsychotic used, n (%) Olanzapine Quetiapine [*patient 3]	8 (89%) 1 (11%)
PICU days at time of antipsychotic initiation, median (IQR)	15 (11-19)
Duration of treatment in days, median (IQR)	13 (9-38)

Table 2: Potential Confounding Factors

Patient #	Withdrawal (WAT ≥ 4)	Extubated*	Antibiotics Prior to Intubation
1	N/A	D5-7	No
2	D6	D3-7	Yes
3*	D5	D3-7	Yes
4	D4-6	N/A	Yes
5	N/A	No	No
6	N/A	D3-7	Yes
7	D4	D4-7	Yes
8	D2	No	No
9	N/A	D7	No

*D = day; N/A = not applicable

Table 3: Effect of Antipsychotic on CAPD Scores

Patient #	Average CAPD Days 1-3	Average CAPD Days 5-7	%Change
1	10.83	10.67	-1.5%
2	11.67	9.33	-20.0%
3*	19.17	12.00	-37.4%
4	9.00	10.83	20.4%
5	18.67	20.75	11.2%
6	15.25	2.33	-84.7%
7	9.67	6.50	-32.8%
8	12.67	16.83	32.9%
9	8.83	8.33	-5.7%

Wilcoxon signed-rank test
Median -10.75, p = 0.43; 95% CI [-43.1 - 15.7]

Figure 1: Effect of Benzodiazepine Dose on Average CAPD Scores D1-3 vs D5-7

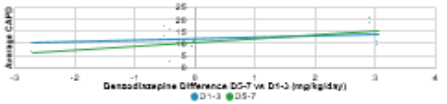


Figure 2: Effect of Opioid Dose on Average CAPD Scores D1-3 vs D5-7

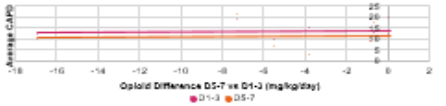
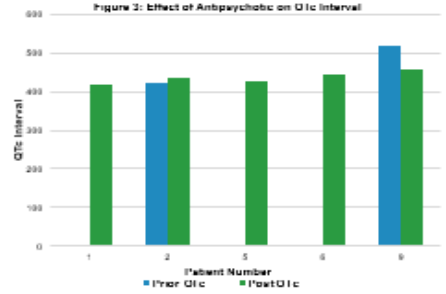


Figure 3: Effect of Antipsychotic on QTc Interval



Discussion

- 44% of patients had > 10% improvement in CAPD scores following initiation of antipsychotic (Table 3)
  - 75% of those patients also had a reduction in benzodiazepine and opioid use (Figure 1)
- Other confounding factors likely contributed to change in CAPD scores (Table 2)
- Limitations
  - Lack of CAPD score documentation
  - Inconsistent practice for obtaining electrocardiograms
  - Small sample size
  - Not all confounding factors assessed

Conclusion

- Primary outcome of change in CAPD scores following initiation of antipsychotic was not statistically significant
- No clinically significant increase in QTc interval was observed
- Continue non-pharmacologic measures for prevention and treatment
- Antipsychotic treatment may continue to be considered in pediatric patients with refractory hyperactive delirium

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Evaluation of Atypical Antipsychotics for Treatment of Delirium in the Pediatric Intensive Care Unit (PICU)
Brianna Henson, PharmD; John Donnelly, PharmD; Mary Subramanian, PharmD, BCPS, BCPPS; Lauren Wyatt, PharmD

Evaluation of blood counts in cystic fibrosis patients who received lumacaftor/ivacaftor: a cystic fibrosis transmembrane conductance regulator

Stephanie M. Yasechko, PharmD Candidate 2020, Kimberly Novak, PharmD, BCPS, BCPPS, FPPA
Nationwide Children's Hospital Department of Pharmacy
Columbus, Ohio

Background

- Adult and pediatric cystic fibrosis (CF) patients at Nationwide Children's Hospital have been anecdotally observed to experience marked reductions in both white blood cells (WBC) and/or platelets while receiving cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapy.
- Currently, no literature exists to support this association.
- Increased immunosuppression could become problematic in CF patients, considering their inability to eradicate bacteria in the lungs.

Objective

- Evaluate our institution's hematologic monitoring practices and to determine the incidence of hematologic abnormalities in patients on CFTR modulator therapy.
- This project reviewed a subset of patients receiving lumacaftor/ivacaftor.

Methods

- This quality improvement project (IRB exempt) involved a retrospective chart review of selected patients at our CF center receiving lumacaftor/ivacaftor.

Inclusion Criteria

- Adult and pediatric patients ages 2 years and older with a confirmed diagnosis of CF
- Receipt of lumacaftor/ivacaftor for at least one month between July 2, 2015 and September 30, 2019
- Baseline CBC within one year of therapy initiation and comparator CBC while on therapy
- First exposure to lumacaftor/ivacaftor

Exclusion Criteria

- Lacking baseline and/or comparator CBC
- Subsequent lumacaftor/ivacaftor exposures after switching back from other CFTR modulator therapies
- Unclearly documented therapy initiation and completion times within the EMR

- Mean baseline WBC and platelet counts from one year prior to the start of therapy were compared with mean WBC and platelet counts while on therapy.

Results

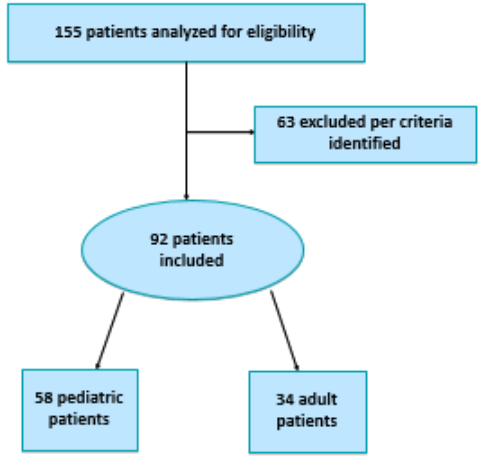

Figure 1. Patient screening flowchart

	Pediatric Patients (N=58)	Adult Patients (N=34)
Age, mean years (range)	10.9 ± 4.4 (2-19)	27 ± 7.7 (20-48)
Sex, N (% male)	28 (48.3%)	19 (55.9%)
Race, N (% white)	57 (98.3%)	33 (97.1%)
F508del/F508del genotype (%)	58 (100%)	34 (100%)
Time on therapy, mean months (range)	29.2 ± 13.7 (3-51)	31 ± 15.2 (2-51)

Table 1. Baseline demographics

	Pre-Treatment Mean WBC	On-Treatment Mean WBC
Pediatric Patients	9.1 ± 3.2	12.5 ± 33.5
Adult Patients	10.4 ± 2.6	10.3 ± 3.4

Table 2. Mean WBC counts (10,000 cells/cubic mm). 4 pediatric and 0 adult patients were identified to have "low" mean average WBC counts while on therapy. Low defined as WBC<5

	Pre-Treatment Mean Platelets	On-Treatment Mean Platelets
Pediatric Patients	306.3 ± 98	327.1 ± 90.9
Adult Patients	298.3 ± 86.7	315 ± 100

Table 3. Mean platelet counts (10,000 cells/cubic mm). 1 pediatric and 1 adult patient was identified to have a "low" mean average platelet count while on therapy. Low defined as platelets<150

Conclusions

- Administration of lumacaftor/ivacaftor did not appear to be associated with a significant reduction in WBC or platelets in either the adult or pediatric cystic fibrosis populations at Nationwide Children's Hospital. However, there were individual outliers as described above.
- Appropriate and vigilant hematologic monitoring should always be utilized for these patients, especially if they are concurrently receiving immunosuppressants.
- More studies will be needed to further explore this question in relation to the other CFTR modulator therapies on the market.

Discussion

Limitations:
- This study was retrospective.
- Concomitant drug therapy was not evaluated.

Future Directions:
- Pending statistics and other CFTR modulator therapy evaluations.

Disclosures

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Evaluation of Atypical Antipsychotics for Treatment of Delirium in the Pediatric Intensive Care Unit (PICU)
Stephanie M. Yasechko, PharmD Candidate 2020, Kimberly Novak, PharmD, BCPS, BCPPS, FPPA

Evaluation of romiplostim utilization in children with chemotherapy-induced thrombocytopenia at a large, academic children's hospital

Emma L. Wysocki, PharmD, RDN, CNSC; Alexis Kuhn, PharmD, BCOP
Nationwide Children's Hospital Department of Pharmacy

Background

Treatment options for chemotherapy-induced thrombo-cytopenia (CIT) are limited

CIT can result in therapy delays, dose reductions, and significant bleeding

Platelet transfusion is the most common treatment for CIT but has many undesirable side effects[1]

Romiplostim, a thrombopoietin receptor agonist effective at raising platelet counts, is FDA-approved for treatment of chronic immune thrombocytopenia in children and adults[2]

Romiplostim has been effective in off-label use for CIT treatment in adults[3]

Data on romiplostim use in pediatric patients with CIT is lacking

Objective

Evaluate the utilization, effectiveness, and safety of romiplostim for CIT in pediatric patients at a large, academic children's hospital

Methods

Retrospective chart review of patients ≤ 18 years of age with CIT who received at least one dose of romiplostim at Nationwide Children's Hospital between January 1, 2014 and July 31, 2019.
The following data was collected;

- Baseline characteristics
- Platelet threshold for treatment or surgery
- Initial dose, dose changes, number of doses, and reason for discontinuation of romiplostim
- Major safety events (bleeding, thrombosis)
- Platelet counts during romiplostim therapy

Results

Table 1. Baseline Characteristics (N = 16)

Age, years	8.8 (3.7)
Female:Male	7:9
Baseline platelets (x10⁹/L)	36 (42)
Received > 1 course	5 (31.3)
Cancer, n (%)	
Neuroblastoma	7 (43.8)
Central nervous system tumor	3 (18.8)
Wilm's tumor	2 (12.5)
Ewing's sarcoma	1 (6.3)
Rhabdomyosarcoma	1 (6.3)
Acute lymphoblastic leukemia	1 (6.3)
Rhabdoid tumor	1 (6.3)

All data presented in mean (SD), median (IQR), or n (%)

Figure 1. Reason for Romiplostim Discontinuation (N = 26)

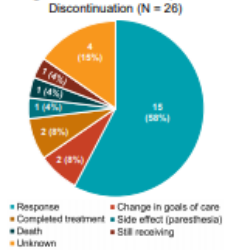
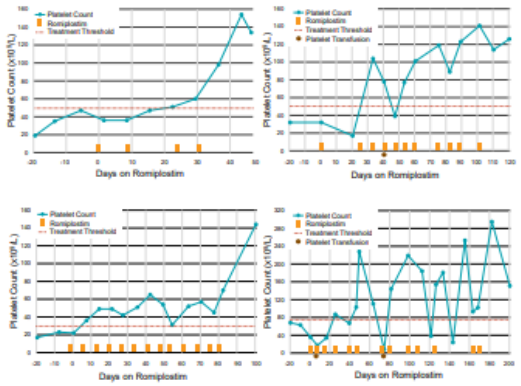


Figure 2. Key Findings

Initial dose (mcg/kg)	Doses per course (n)	Dose to reach threshold (mcg/kg)	Platelet threshold achieved (n)	Thrombosis (n)	Bleeding, Grade 1 (n)	Bleeding, Grade 2 (n)
4.3 (1.8)	6.5 (5.5)	5.3 (2.2)	20 (76.9)	0 (0)	5 (18.5)	1 (3.8)

All data presented in mean (SD) or n (%)

Figure 3. Platelet Response to Romiplostim for Select Patients



- Twenty-six treatment courses among 16 patients were included in this analysis
- The majority of patients (77%) achieved their platelet threshold while receiving romiplostim
- Concomitant platelet transfusion was common (81%)
- The average dose required to achieve platelet threshold was 5.3 mcg/kg
- No patients in this analysis experienced thrombosis during treatment and one patient experienced a major bleeding event

Conclusion

Romiplostim, in combination with platelet transfusion, was effective in increasing platelet counts above thresholds for the majority of patients in this analysis

Romiplostim was well tolerated with no incidence of thrombosis and only one patient with discontinuation due to side effects (paresthesia)

Romiplostim, in combination with platelet transfusion, may be considered as a treatment option in pediatric patients with refractory chemotherapy-induced thrombocytopenia

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Disclosures

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Evaluation of romiplostim utilization in children with chemotherapy-induced thrombocytopenia at a large, academic children's hospital
Emma L. Wysocki, PharmD, RDN, CNSC; Alexis Kuhn, PharmD, BCOP

Evaluation of ursodiol use in patients with cystic fibrosis

Catherine Mechler, PharmD Candidate and Kimberly J. Novak, PharmD, BCPS, BCPPS, FPPA

Nationwide Children's Hospital Department of Pharmacy

Background

- Cystic fibrosis (CF) is the most common genetic disease for Caucasians[1]
- Patients with CF often have gastrointestinal, pancreatic, and hepatobiliary diseases secondary to chloride channel dysfunction[1]
- Ursodiol is a gallstone dissolution agent that is often prescribed for some of these complications[2], including:
  - Liver disease related to CF – confirmed or increased liver function tests (LFTs)
  - Gallbladder (GB) cholestasis
  - Total parenteral nutrition (TPN)-induced cholestasis
- There is a lack of strong evidence promoting the routine use of ursodiol[3] and it can increase the risk of adverse reactions
- Ursodiol often remains on a patient's medication list even after it is no longer indicated, causing higher pill burden, increased risk for drug-drug interactions, and higher cost to the patient

Objectives

Primary Objective

- Evaluate the proportion of cystic fibrosis patients taking ursodiol when it may no longer be indicated

Secondary Objectives

- Analyze the initial indication of patients with opportunity for ursodiol removal
- Analyze the initial indication of cystic fibrosis patients who were taking ursodiol, but correctly taken off

Methods

Retrospective Chart Review

- IRB expedited review
- Descriptive statistics used for analysis

Inclusion/Exclusion Criteria

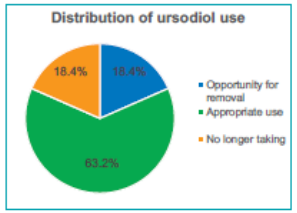
- Cystic fibrosis patients receiving ursodiol
- No exclusions were needed for assessment
- January 1, 2014 - July 31, 2019

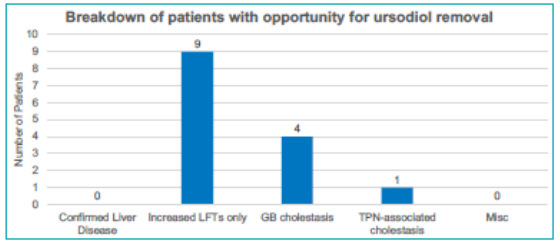
Data Collected

- Pediatric/adult patient care team designation
- Sex
- Cystic fibrosis mutation
- Length of treatment duration
- Initial ursodiol indication

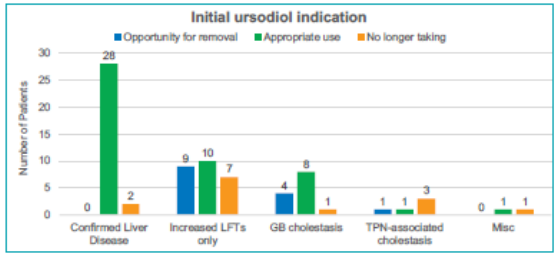
Results

Demographics (N = 76)	
Pediatric, n (%)	35 (46)
Male, n (%)	38 (50)
CF mutation	
Homo-F508del, n (%)	37 (48.7)
Hetero-F508del, n (%)	9 (11.8)
Other, n (%)	2 (2.6)
Not classified, n (%)	28 (36.8)





Initial Indication Categories (N = 76)	
Mean treatment duration, years (range)	6 (0 – 18)
Initial ursodiol indication	
Confirmed liver disease, n (%)	30 (39.5)
Increased LFTs only, n (%)	26 (34.2)
Gallbladder cholestasis, n (%)	13 (17.1)
TPN-associated cholestasis, n (%)	5 (6.6)
Other, n (%)	2 (2.6)



Discussion

- There are quite a few patients (18.4%) that could be candidates for the removal of ursodiol from their medication list
- Of this group that was flagged for possible ursodiol removal, 64.3% of them (9 of 14) were initially started due to elevated liver enzymes which have since resolved
- Seven of the fourteen patients (50%) that are no longer taking ursodiol were stopped after their liver enzymes normalized for at least 6 months
- Other reasons to potentially discontinue ursodiol therapy included resolution of TPN-induced cholestasis after discontinuing TPN, and resolution of cholestasis after cholecystectomy

- **Limitations:**
  - Small sample size (N = 76)
  - Subjective interpretation of indication of therapy based on chart documentation
  - Progression in disease can change initial indication for ursodiol
  - Medication lists are not always up-to-date, especially if the patient receives primary care elsewhere

Conclusions

- The prevalence of continued prescribing of ursodiol when it is no longer indicated is relevant
- When the initial ursodiol indication is for elevated liver enzymes, it is important to continuously reassess the patient's need for this medication

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Evaluation of ursodiol use in patients with cystic fibrosis
Catherine Mechler, PharmD Candidate and Kimberly J. Novak, PharmD, BCPS, BCPPS, FPPA

Implementation of a penicillin oral dose-graded challenge without skin testing at an academic pediatric institution

Mara Rubin, PharmD; Jessica Tansmore, PharmD; Juan D. Chaparro, MD; Jessica Hehmeyer, MHA; Charlie Macias, MHA; Joshua Watson, MD; Maria Vegh, RN, MSN, CPN; David Stukus, MD

Nationwide Children's Hospital, Columbus, Ohio

Background

Self-reported penicillin allergies are highly prevalent:[1]
- Between 70-90% are mislabeled

Compared with adults, pediatric penicillin allergies are:[1-2]
- More commonly a result of viral-induced exanthems
- Less likely to be a serious allergic reaction

Penicillin allergy mislabeling impacts:[1]
- Antibiotic appropriateness, treatment efficacy, duration, adverse effects, and expense
- Antibacterial resistance and antimicrobial stewardship

Penicillin allergy skin testing:[2-3]
- Historically recommended prior to oral challenges to reduce risk of severe acute challenge reactions
- Resource- and time-intensive
- High rate of false positives

Penicillin oral dose-graded challenges:[1, 4-7]
- Appropriate for non-IgE and delayed-onset adverse reactions
- Specificity of 100%, negative predictive value of 89.1%, and positive predictive value of 100%
- Limited to prolonged courses as an outpatient

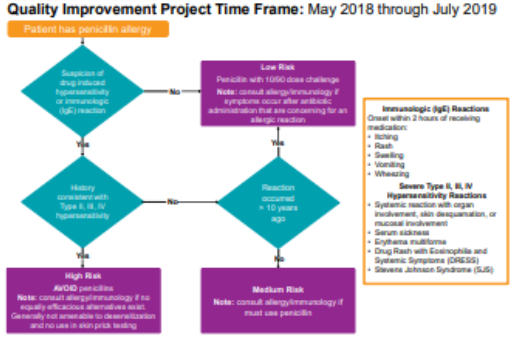
Objectives

Primary Objective
- Implement penicillin oral dose-graded challenges without prior skin testing

Secondary Objective
- Remove documented penicillin allergies from the electronic medical record

Methods

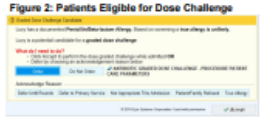
Quality Improvement Project Time Frame: May 2018 through July 2019



Methods Continued

Figure 1: Nursing Questionnaire

Figure 2: Patients Eligible for Dose Challenge



Results

Figure 3: Penicillin Allergies Removed Prior to Discharge

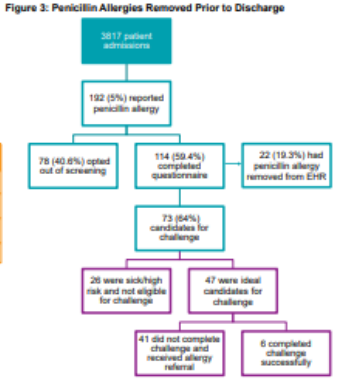
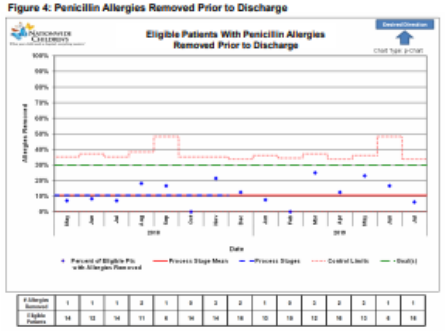


Table 1: Recorded Penicillin Allergies of Patients Who Completed Questionnaire

Penicillin Antibiotic	Number of Patients With Allergy	Percentage of Patients With Allergy
Amoxicillin	69	60%
Penicillin	36	32%
Amoxicillin-Clavulanate	9	8%
Total	114	100%

Figure 4: Penicillin Allergies Removed Prior to Discharge



Limitations

- Results reflective of oral dose-graded challenges completed through the electronic medication record order-set
- One-to-one nursing is required to execute the challenge
- Allergies listed as intolerances were not included and likely to be eligible for the challenge
- Current screening tool triggers to re-evaluate each patient during each admission, so total eligible patients may be falsely elevated

Conclusions

- Pediatric patients with mild, non-IgE reported penicillin allergies are an appropriate patient population for an oral dose-graded challenge without prior skin testing
- Penicillin oral dose-graded challenges in the inpatient setting provide an opportunity to clarify reported penicillin allergies

Future Directions

- Expand the dose challenge to other inpatient units and outpatient settings to target more eligible patients
- Expand scope of antibiotics to include intravenous formulations and other beta-lactams including cephalosporins and carbapenems
- Retrospective review of patients who passed an oral dose-graded challenge and if they have received the drug subsequent to removal of their previously reported allergy

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Implementation of a penicillin oral dose-graded challenge without skin testing at an academic pediatric institution
Mara Rubin, PharmD; Jessica Tansmore, PharmD; Juan D. Chaparro, MD; Jessica Hehmeyer, MHA; Charlie Macias, MHA; Joshua Watson, MD; Maria Vegh, RN, MSN, CPN; David Stukus, MD

Integrated pharmacy automation management reduced formula usage and improved exclusive breastfeeding rates in a *Baby Friendly* community hospital

David M. Dirig, Leonid Sokolskiy, Maria Itani, Tammy Turner, and Tracey Ybarra
Martin Luther King, Jr. Community Hospital, Los Angeles, CA; Cardinal Health, Houston, TX

Martin Luther King, Jr. Community Hospital

CardinalHealth *Essential to care™*

Background

- MLKCH is a 131-bed safety-net community hospital that opened in 2015.
- Greenfield build in 2014; *Baby-Friendly Hospital Initiative* participation since 2016.
- Level One Perinatal Department averages 60 neonates monthly.
- Founding state (baby formula)
  - Materials Management stocked baby formula on the nursing unit as supply.
  - Multiple products. High par levels. No utilization tracking.
- Study period (baby formula)
  - Pharmacy took over formula dispensing in September, 2018.
  - Formula options streamlined to a single 2oz (60mL) product.
  - Formula dispensed only from profiled Pyxis MedStation per pediatrician order.

Objectives

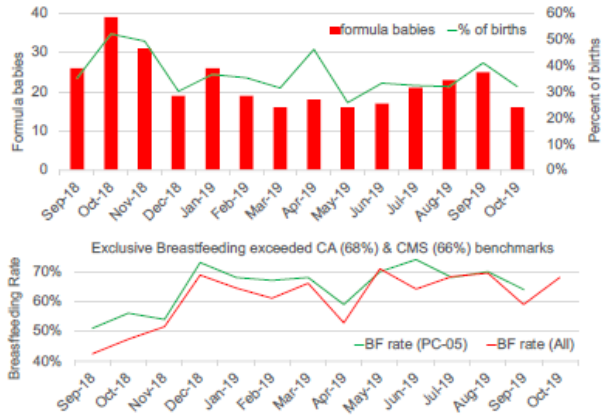
- Leverage automation & electronic health record to manage formula logistics.
- Capitalize on Pyxis analytics to report formula dispensing patterns.
- Reduce formula use and improve exclusive breastfeeding rates.

Methods

- MLKCH Medication Management Automation
  - BD Pyxis ES (MedStation) interfaced to Cerner Millennium (version 2015.23).
- Formula lockdown. *"It's easier to get fentanyl than formula……"*
  - Consensus reached to streamline to a single formula option.
  - Prescriber order required in electronic health record for formula to be given.
  - Formula order built into electronic order set (powerplan) to promote appropriate neonatal nutritional choices. Formula hidden as orderable (no one-off orders).
  - Formula set to auto-verify in PharmNet to prevent review delays in Pharmacy.
  - Dispensed from Pyxis MedStation as profiled item (no override allowed).
  - Clinical Data Category (CDC) designed in Pyxis to query user before removal.
    - *"Have you documented an alternative feeding method using mom's own breastmilk (e.g., spoon, cup, or syringe)?"*
  - Formula treated as a medication and included in Bar Code Med Administration.
- Formula Management Analytics Dashboard
  - Formula dispensing activity (Pyxis) and Cerner patient specifics reported monthly to inform leaders as to personnel ordering and dispensing patterns.
  - Monthly reports on usage, breastfeeding percentage, and frequency analysis.
  - Scatter plot analysis indicated high-use and low-use patterns per neonate.
  - User CDC responses analyzed for appropriate use and formula justification.

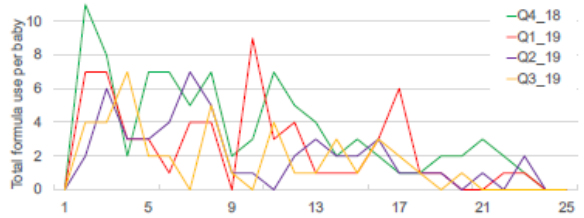
Results – Formula Logistics

Results – Exclusive breastfeeding



Variably-defined Exclusive Breastfeeding : Breastfeeding (All) represents an internal MLKCH measure tracking all babies each month (no exclusions). Exclusive breastfeeding, as defined by CMS/TJC Core Measures PC-05, excludes transfers to higher-level care. *Baby-Friendly* allows exclusion of mothers inappropriate for breastfeeding (e.g., substance abuse or HIV+) or per mother's choice to formula feed when accompanied by risk/benefit education and support to identify and address breastfeeding barriers.

Results – Low-use formula consumption



Education to reduce "onesie-twosies:" Note chronological reduction in "formula babies" receiving ≤3 bottles during hospital stay after implementation of Pyxis CDC. Decreased frequency of low-usage cases correlated with improved exclusive breastfeeding rates.

Summary

- Results of applying automation analytics to formula management included:
  - Formula spend decreased by 70%.
  - Monthly formula usage decreased by 25%.
  - Formula refill and restock workload decreased by 95%.
  - Percent of neonates receiving formula decreased by 30%.
  - Low-usage consumption (≤3 bottles per neonate stay) decreased by 60%.
  - Bar Code Medication Administration scan rate for formula exceeded 95%.
  - Exclusive breastfeeding rates at MLKCH increased by 30%.
  - Exclusive breastfeeding rates exceeded CMS, TJC, & California standards.

Conclusion

MLKCH sought to improve neonatal care by collaborating with the *Baby Friendly Hospital Initiative* to promote breastfeeding and prioritize the use of breast milk over formula. By implementing required ordering of formula by prescribers only via EHR order set, pharmacy dispensing automation, and nursing/medical staff education, formula spend and usage decreased while exclusive breastfeeding rates increased without adversely affecting prescriber, pharmacy, or nursing staff workflow.

Disclosures

The authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: David Dirig – Nothing to disclose; Leonid Sokolskiy – Nothing to disclose; Maria Itani – Nothing to disclose; Tammy Turner – Nothing to disclose; Tracey Ybarra – Nothing to disclose.

Integrated pharmacy automation management reduced formula usage and improved exclusive breastfeeding rates in a Baby Friendly community hospital
David M. Dirig, Leonid Sokolskiy, Maria Itani, Tammy Turner, and Tracey Ybarra

Intravenous methylnaltrexone for the treatment of opioid-induced constipation in critically ill pediatric patients

Kimberly Johnstone, PharmD; Christopher McPherson, PharmD, BCPPS; Ahmed Said, MD, PhD; Michael Lahart, PharmD, BCPPS
St. Louis Children's Hospital, St. Louis, MO

12-096

Background

- Methylnaltrexone is a peripherally acting mu-opioid receptor antagonist that is indicated for adults with Opioid-Induced Constipation (OIC) in chronic non-cancer pain and OIC in advanced illness
- Critically ill pediatric patients may benefit from its use
- There is a paucity of data describing the safety and efficacy of intravenous methylnaltrexone in critically ill pediatric patients

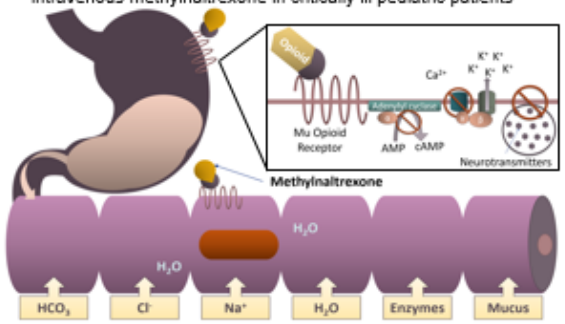


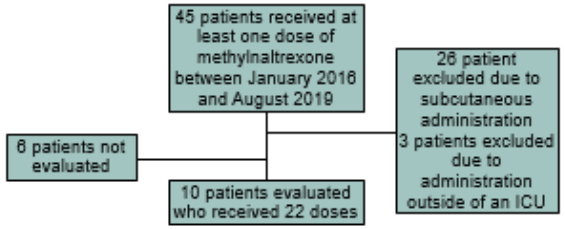
Figure 1. Mechanism of action of methylnaltrexone in OIC

Objective

The primary objective is to evaluate the safety and efficacy of methylnaltrexone via intravenous injection in treating OIC in critically ill pediatric patients.

Methods

Study procedures were approved by the Institutional Review Board of Washington University in St. Louis.



Response to methylnaltrexone was defined as a documented laxation within 24 hours of methylnaltrexone administration.

Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
All authors: Nothing to disclose

Preliminary Results

Table 1. Patient Characteristics and Response to Methylnaltrexone in Intensive Care Unit Setting

Age	Sex	Clinical Status	Surgery (30 days prior)	Abdominal Disease	Opioid Duration (Days)	MNTX Dose (mg/kg)	MME/kg 24 Hours Prior	Total Doses	Response to First Dose	Response to a Dose	Adverse Event(s)
7 months	M	Intubated	NO	NO	31	0.16	2.3	1	NO	NO	YES (emesis)
2 years	M	Tracheostomy	NO	NO	12	0.15	0.3	3	YES	YES	NO
8 years	F	Intubated, CRRT, ECMO	YES	NO	17	0.16	0.9	5	YES	YES	NO
5 years	M	Intubated, CRRT	NO	YES	5	0.15	0.5	4	NO	YES	NO
8 years	F	Intubated, ECMO	NO	NO	20	0.11	3.5	2	NO	YES	YES (abdominal pain)
9 years	F	Intubated	YES	NO	10	0.15	9.4	3	NO	YES	NO
18 years	F	Intubated, CRRT, ECMO	NO	NO	31	0.15	5.6	1	YES	YES	NO
5 months	M	Intubated	YES	YES	12	0.16	19.1	1	YES	YES	NO
1 year	F	Post cardiac arrest, OHT	YES	NO	92	0.16	0.2	1	YES	YES	NO
8 years	M	Pain crisis	NO	YES	N/A	0.14	1.7	1	YES	YES	YES (emesis)

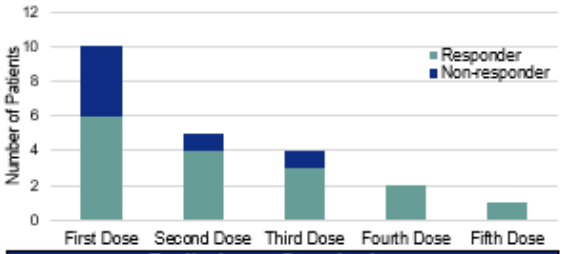
MME = morphine milligram equivalents
MNTX = methylnaltrexone
OHT = orthotopic heart transplant

Table 2. Patient Characteristics at Time of Dose Administration

	Doses with Response (n=16)	Doses without Response (n=6)	P value
Number of laxatives 24 hours prior to MNTX	3 (2-4)	3 (2-5)	0.91
Time since laxation (hours)	18 (11-56)	16 (3-37)	0.60
Time to laxation after dose (hours)*	7 (3-17)	42 (30-62)	< 0.001
Enteral nutrition prior to dose	2 (13%)	2 (33%)	0.29
Enteral nutrition after dose	6 (38%)	3 (50%)	0.66
Number of laxation(s) 24 hours after dose*	3 (1-4)	0 (0-1)	0.001
rFLACC 24 hours prior to administration	0 (0-4)	1 (0-1)	0.80
rFLACC 24 hours after administration	0 (0-2)	1 (0-3)	0.72
Concomitant medications			
Anti-emetics	1 (6%)	0	1
Inotropes	2 (13%)	0	1
Paralytics	1 (6%)	1 (17%)	0.48
Sedatives	13 (81%)	6 (100%)	0.53
Vasopressors	7 (44%)	2 (33%)	1
Vasodilators	3 (19%)	1 (17%)	1

Values reflect median (IQR) or number (percent)
*Statistical significance
rFLACC = revised face, legs, activity, cry consolability scale

Figure 2. Patient Response to Methylnaltrexone Administration Based on Number of Doses



Preliminary Conclusions

- Intravenous methylnaltrexone dosed at 0.15 mg/kg appears to be safe and effective in treating OIC in critically ill pediatric patients, with 60% of patients responding to the first dose and 76% to all doses
- Single doses and repeated dosing of methylnaltrexone were well tolerated
- Patients responded to methylnaltrexone over a wide variety of opioid requirements and durations prior to administration
- Methylnaltrexone was safely administered to patients with varying clinical status, postoperatively, and underlying abdominal disease

Presented at the 54th American Society of Health-System Pharmacists Midyear Clinical Meeting on December 11, 2019 in Las Vegas, Nevada

Intravenous methylnaltrexone for the treatment of opioid-induced constipation in critically ill pediatric patients
Kimberly Johnstone, PharmD; Christopher McPherson, PharmD, BCPPS; Ahmed Said, MD, PhD; Michael Lahart, PharmD, BCPPS

Medication use evaluation of eculizumab at a free-standing pediatric institution

Christopher R.T. Stang, PharmD and Michael Storey, PharmD, MS, BCPS

Nationwide Children's Hospital Department of Pharmacy

Background

- Eculizumab is a monoclonal antibody that binds to complement protein C5 resulting in the inhibition of terminal complement complex
- This inhibition has been used off label for processes such as intravascular hemolysis, thrombotic microangiopathy (TMA) post-bone marrow transplant (BMT), and solid organ transplant rejection (SOTR)
- The only FDA approved pediatric indication for eculizumab with specific weight-based dosing is atypical hemolytic uremic syndrome (aHUS)
- Eculizumab is recommended to be given via intravenous infusion over 35 minutes in adults and 1-4 hours in pediatric patients
- Patients receiving concomitant plasmapheresis, plasma exchange, or infusions of fresh frozen plasma are recommended to receive supplemental doses of eculizumab
- Eculizumab therapy is associated with an increased risk of infections, most notably meningitis and encapsulated bacterial infections, thus it's recommended to receive the meningococcal vaccine two weeks prior to initiation of therapy
- At Nationwide Children's Hospital, eculizumab is utilized for various indications by different services
- There is no consensus pediatric dosing recommendations for eculizumab when used for indications outside of aHUS

Objectives

Primary

- Evaluate dosing, indications, and service lines utilizing eculizumab

Secondary

- Monitor safety and efficacy of eculizumab

Methods

- Single center retrospective chart review
- **Inclusion Criteria:**
  - Patients who received eculizumab between August 1st, 2013 and August 1st, 2019
  - Eculizumab administered during inpatient admissions and outpatient infusion clinics
- Patient demographics, therapy characteristics, safety, efficacy and logistical data points were collected from the electronic medical record
- Descriptive statistics were utilized for all analyses
- The Institutional Review Board determined this study to be quality improvement and did not require a formal review

Results

Table 1. Patient Demographics (n = 25)

Median Age, years	8.8
Range	0.58 – 25.29
Median Weight, kg	32.2
Male, n (%)	13 (52)

Table 2. Therapy Initiation

Initiation Location (n)	
Inpatient	20
Infusion Clinic	5
Initial Infusion Time (n)	
35 minutes	6
60 minutes	14
120 minutes	3
180 minutes	2

Table 4. Initial Dosing by Indication

aHUS	
Patients dosed per PI, %	100
Complement-Mediated SOTR	
10 kg to <20 kg, dose (n)	600 mg (1)
>40 kg, dose (n)	1200 mg (3)
TMA	
10 kg to <20 kg, dose (n)	600 mg (5)
20 kg to <30 kg, dose (n)	600 mg (1)
30 kg to <40 kg, dose (n)	900 mg (1)
>40 kg, dose (n)	600 mg (1) 1200 mg (4)

PI – package insert

Figure 1. Management of Dose Altering Instances

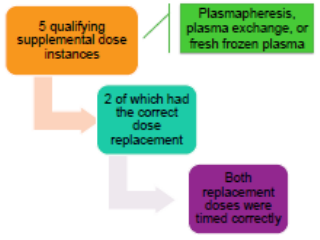


Table 3. Therapy Characteristics

Indication (n)	
TMA post- BMT	12
aHUS	7
Complement-mediated SOTR	4
Other	2
Ordering Service (n)	
Bone marrow transplant	12
Nephrology	7
Transplant service	4
Hematology/Oncology	1
Pediatric critical care	1
Length of Therapy	
Total doses administered, median	11
Length of therapy, months, median	3

Table 5. Use and Efficacy

Alive at 1 year,* n (%)	17 (77)
Death(s) by indication	
TMA	4 deaths
Complement-mediated rejection (heart)	1 death
Indication for Discontinuation* (n = 22)	
Defined criteria, n (%)	11 (55)
No defined criteria, n (%)	8 (40)
Death, n (%)	3 (15)
No incidences of TMA were observed following discontinuation of eculizumab	

*Excluded patients too soon to evaluate (n = 3)

Table 6. Safety

Meningococcal vaccine prior to first dose, n (%)	13 (52)
No cases of meningococcal infection were detected during chart review	

Discussion

- Most patients were initiated on eculizumab while inpatient, likely the result of acute processes that eculizumab was used to treat
- Ordering service was aligned with their respective indication: BMT and TMA, nephrology and aHUS, and transplant services and complement-mediated SOTR

Dosing

- Initial doses were largely consistent with labeled dosing for pediatric aHUS
- Patients receiving supplemental doses were timed appropriately
  - Several patients did not receive supplemental doses

Safety

- Under half of patients did not receive a meningococcal vaccine prior to the first dose
  - This likely reflects the complex, acute nature in which patients needed eculizumab therapy in this cohort
- A large portion of patients did not have clearly defined discontinuation criteria
- The majority of patients survived to one year after therapy initiation, with most of the deaths occurring in patients with TMA

Limitations

- Patients receiving eculizumab via home health care were not detected by the initial report
- Lack of documentation created difficulty assessing the need for supplemental doses
- Only labeled recommendations for meningococcal prophylaxis were evaluated
  - Consults to infectious disease and antibiotic prophylaxis were observed

Conclusions

- Most patients received eculizumab off-label, which is expected given the population studied in this review
- Generally the initiation of eculizumab utilized doses similar to approved dosing nomograms
- Meningococcal prophylaxis was provided when possible
- A lack a defined treatment parameters and goals were common, with few indications for discontinuation
- No safety signals were observed

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Medication use evaluation of eculizumab at a free-standing pediatric institution
Christopher R.T. Stang, PharmD and Michael Storey, PharmD, MS, BCPS

Pediatric emergency department acute agitation pharmacological management pathway update

Anna Dugovich, PharmD Candidate 2021, Kimberly Shipp, PharmD, BCPS, BCPPS, Lauren Yates, PharmD and Meredith McCauley, PharmD
Department of Pharmacy, Nationwide Children's Hospital, Columbus, Ohio

Purpose

To maximize the safety and efficacy of acute agitation medication use in the emergency department (ED) at a pediatric teaching hospital

Background

- Acute agitation is a state of behavioral dyscontrol that will likely result in harm to the patient or healthcare workers without intervention[1]
- Despite the lack of clear guidelines, a standardized pathway can help enhance safety and efficacy of acute agitation medications used
- Nationwide Children's Hospital (NCH) uses an acute agitation pathway in the ED which includes the treatment options outlined in Figure 1

Figure 1. Acute Agitation Medications on Current Pathway

Oral Options
- Risperidone: 0.5 mg (<45 kg) or 1 mg (>45 kg)
- Lorazepam: 0.05-0.1 mg/kg/dose (max 4 mg)
- Can give extra dose of home antipsychotic if appropriate

IM Options
- Lorazepam: 0.05-0.1 mg/kg/dose (max 4 mg)
- Haloperidol: 2 mg (<45 kg) or 5 mg (>45 kg)
- Diphenhydramine PO/IM: 1 mg/kg/dose (max 50 mg) recommended with haloperidol for prophylaxis of extrapyramidal symptoms (EPS)

- Possible areas of improvement within the current pathway include:
  1. Minimize sedation risk with medication administration to decrease time to patient evaluation
  2. Increase medication options with evidence in agitation to allow for individualization based on etiology of agitation
  3. Decrease risk of EPS with antipsychotic administration to avoid unnecessary discomfort for patient

Methods

- Review literature to find current evidence on methods to treat acute agitation in pediatric patients
- Collaborate with pharmacists and a psychiatrist to review information
- Finalize changes with agreement from Psychiatry and ED staff

Results

1. Minimize Risk of Sedation with Medication Administration
- Management of agitation must be balanced with the risk of sedation associated with use of antipsychotics and benzodiazepines (BZD)[2]
- Utilization of lowest effective dose for agitation minimizes risk of sedation
- A maximum dose of 2 mg for lorazepam orally or intramuscularly is recommended to manage agitation while avoiding over-sedation[2]

2. Additional Medication Options with Evidence in Agitation
- Agitation is a symptom and treatment should be individualized based on patient specific etiology whenever possible[2]

Figure 2. Summary of Evidence Based Medication for Agitation[2-4]

Indication	Medication
Delirium	- Quetiapine PO, risperidone PO, ziprasidone IM, olanzapine PO/IM - Clonidine only if antipsychotics are contraindicated - Avoid benzodiazepines
Developmental Delay	- Avoid IM medications for safety and BZD (risk of disinhibition) - Antipsychotics or diphenhydramine can be used
Intoxication or Withdrawal	- Alcohol/BZD withdrawal or stimulant intoxication: lorazepam PO/IM, diazepam PO, chlordiazepoxide PO - Alcohol/BZD intoxication: haloperidol IM
Psychosis	- Risperidone PO, quetiapine PO, olanzapine IM, haloperidol +/- BZD IM, ziprasidone IM
Anxiety, PTSD or Trauma	- Lorazepam PO/IM - Clonidine (if <12 y/o or history of disinhibition with BZD)
Unknown Etiology	- Moderate agitation: lorazepam PO/IM, diphenhydramine PO/IM, olanzapine PO/IM - Severe: haloperidol + BZD PO/IM, olanzapine PO/IM, ziprasidone IM

3. Decrease EPS Risk with Antipsychotic Administration
- Antipsychotics, especially those with higher potency, have the potential to cause acute dystonic reactions (AdR), a type of EPS[2]
- AdR can be frightening for the patient and degrade the relationship between patient and doctor[5]
- Diphenhydramine can be used as prophylaxis or treatment for AdR[3] but has risk for increased sedation[2]
- Usual diphenhydramine dose is 1 mg/kg/dose (max 50 mg) but there is little information on if a lower dose could be used for EPS prophylaxis
- Benztropine can also be used as prophylaxis or treatment of AdR[3] at a dose of 0.02-0.05 mg/kg/dose (max 2 mg) with a lower chance of sedation

Figure 4. Acute Dystonia Risk Factors[6]
- History of Dystonia
- High Potency Antipsychotic
- Male Gender
- Age 10-19
- Recent Cocaine Use
- IM Administration

Conclusions

1. Minimize Risk of Sedation with Medication Administration
- Decrease lorazepam to lowest effective dose for agitation
  Current: Lorazepam 0.05-0.1 mg/kg/dose (max 4 mg)
  Proposed Change: Lorazepam 0.05 mg/kg/dose (max 2 mg)

2. Additional Medication Options with Evidence in Agitation
- Due to evidence in agitation, add oral olanzapine and risperidone and intramuscular ziprasidone
  Current: Risperidone PO: 0.5 mg (<45 kg), 1 mg (>45kg); haloperidol IM: 2 mg (<45 kg), 5 mg (>45 kg)
  Proposed Additions: Ziprasidone IM: 5-10 mg; olanzapine PO: 2.5-10 mg
- Add guidance for etiology driven medication selection

3. Decrease EPS Risk with Antipsychotic Administration
- Due to increased risk of EPS with high potency antipsychotics, add low dose diphenhydramine as required prophylaxis when administering intramuscular haloperidol
  Current: Diphenhydramine PO/IM: 1 mg/kg/dose (max 50 mg) recommended prophylaxis with haloperidol administration
  Proposed Change: Diphenhydramine IM 0.5 mg/kg/dose (max 25 mg) or benztropine 0.02-0.05 mg/kg/dose (max 2 mg) with IM haloperidol administration

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Pediatric emergency department acute agitation pharmacological management pathway update
Anna Dugovich, PharmD Candidate 2021, Kimberly Shipp, PharmD, BCPS, BCPPS, Lauren Yates, PharmD and Meredith McCauley, PharmD

Pharmacist impact on medication reconciliation in patients discharged from a pediatric complex care inpatient service

Elaine Yung, PharmD; Dan Rieck, PharmD; Kayla Petkus, PharmD, BCACP

Nationwide Children's Hospital Department of Pharmacy, Columbus, OH

Background

- Inaccurate medication lists lead to an increased risk of medication-related errors
- 21% of all reported of adverse drug events in 2018 were from the Complex Care service at a large free-standing pediatric hospital
- >95% of admitted patients have their medications reviewed daily by a inpatient pharmacist
- Joint Commission requires that medication reconciliation occur at admission, each transition of care, and discharge
- Pharmacists have the knowledge to assist in providing medication reconciliation

Objectives

Primary Objective:
Determine the impact of pharmacist interventions on the reduction of medication-related errors during discharge medication reconciliation for Complex Care patients transitioning from hospital to community settings

Secondary Objectives:
- Examine types of medication-related errors
- Quantify risk of medication-related errors associated with multiple floor transfers during the hospital admission

Methods

Chart reviews of patients discharged from the Complex Care inpatient service at Nationwide Children's Hospital were completed using electronic health records to analyze medication-related errors.

- **Medication-related error**: any preventable error that may lead to inappropriate medication use or patient harm
- **Intervention**: pharmacist and student pharmacist-led discharge medication reconciliations completed Monday - Friday 9am - 5pm

- Pre and post-intervention reviews were evaluated by the same pharmacist

Results

Table 1. Pre-intervention (n=20 patients)	
Transfers	1.8 ± 1.1
Patient age (years)	9.9 ± 8
Male (%)	70
Discharge medications	19.6 ± 6.5
Discharge medication errors	2 ± 2.1

Table 2. Intervention (n=19 patients)	
Transfers	1.5 ± 0.6
Patient age (years)	9.2 ± 6.8
Male (%)	63.2%
Discharge medications	17.6 ± 7.5
Discharge medication errors	0.7 ± 1.1

Table 3. Post-intervention (n=19 patients)	
Remaining discharge medication errors	1.5 ± 2

Figure. 1. Medication Errors, n=39 patients

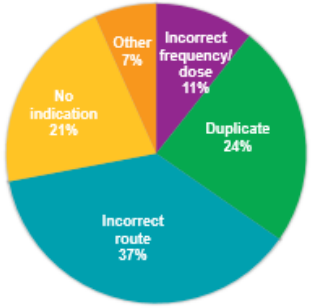

Table 4. Transfers during hospital admission	≥3 transfers (n=7 patients)	<3 transfers (n=32 patients)
Discharge medications	21.3 ± 6.5	18 ± 7
Discharge medication errors	2.4 ± 2	1.1 ± 1.6

Discussion

Baseline characteristics were similar between the two groups.

Primary Objective:
- Pharmacy discharge medication reconciliation slightly decreased amount of medication-related errors
- Post-intervention identified documented errors that were unable to be changed before patient discharge

Secondary Objectives:
- Most common error found on discharge medication lists were incorrect routes (37.3%) as Complex Care patients often receive medications via gastric and/or jejunal tubes
- Patients with ≥3 transfers trended higher averages of discharge medications and errors compared to patients transferred <3 times

Study Limitations:
- No standardized documentation process to adjust discharge medication list with errors identified
- Unable to perform discharge medication reconciliations 24/7
- Limited analysis timeframe

Conclusions

Discharge medication reconciliations can help reduce medication-related errors. Although this study did not see a significant difference, additional studies implementing pharmacy-led discharge medication reconciliations should be conducted to demonstrate the reduction in medication-related errors. Per survey of pharmacists, the main obstacles to completing more medication reconciliations is lack of time due to other job responsibilities.

Future Directions:
- Standardize the definition of medication reconciliation and documentation processes
- Determine cost benefit analysis of medication reconciliations
- Identify patients with ≥3 transfers as a population that may be at higher risk for discharge medication errors
- Implement medication reconciliations in multiple inpatient and outpatient services

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Pharmacist impact on medication reconciliation in patients discharged from a pediatric complex care inpatient service
Elaine Yung, PharmD; Dan Rieck, PharmD; Kayla Petkus, PharmD, BCACP

Quantification of Safety Outcomes Associated with Attention Deficit Hyperactivity Disorder (ADHD) Medications in Children and Youth with Special Health Care Needs (CYSHCN)

University of Colorado Anschutz Medical Campus

Lionel Sielatchom-Noubissie[1]; Evan Atchley[1]; Lucas Orth, PharmD, BCPPS[1,2]; Allison Blackmer, PharmD, FCCP, BCPS, BCPPS[1,2]

[1]University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences

[2]Children's Hospital Colorado

Children's Hospital Colorado

Background

- CYSHCN, comprising approximately 16% of all children in the United States[1], may be predisposed to receiving ADHD medications due to a high incidence of behavioral and developmental disorders
- ADHD pharmacotherapies effectively reduce symptoms, but are associated with adverse events (AEs) such as effects on sleep, appetite, and cardiovascular events[2,3]
- AEs may be more pronounced in CYSHCN due to complex comorbidities, polypharmacy, and altered pharmacokinetics & pharmacodynamics[3]
- To date, the safety of ADHD medications has not specifically been evaluated in CYSHCN

Objectives

1. Characterize the subset of CYSHCN receiving ADHD medications
2. Quantify safety outcomes associated with ADHD medications in CYSHCN

Methods

Study Design

- Single-center, retrospective study of CYSHCN:
  - Receiving care at Children's Hospital Colorado Special Care Clinic (SCC) between 1/1/2015—7/31/2019
  - Initiated on ≥1 stimulant or non-stimulant for ADHD management
- Patients were excluded if:
  - Age ≤31 days or ≥21 years during study
  - ADHD pharmacotherapy coordinated entirely outside of the institution
- COMIRB approved

Primary Outcome Measures

- Age, BMI, race, primary insurance, pertinent comorbidities and neurologic impairment

Secondary Outcome Measures

- Incidence of adverse effects, appetite stimulant and sleep aid initiation, and discontinuation data

Statistical Analysis

- Descriptive statistics using REDCap™ reporting tools and Microsoft® Office Excel

Results

Figure 1. Screening, Eligibility, and Study Inclusion

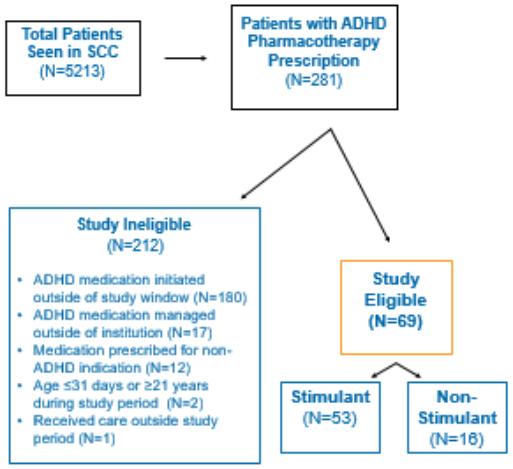


Table 1. Characterization of CYSHCN Prescribed ADHD Medication

Characteristic	Stimulant* N=53	Non-Stimulant† N=16	All N=69
Median Age, yrs (IQR)	8.01 (6.5, 9.4)	10.94 (9.0, 13.9)	8.01 (6.5, 9.6)
Median BMI, kg/m² (IQR)	16.59 (15.2, 19.9) *N=50*	15.11 (14.5, 16.4) *N=15*	16.31 (14.9, 19.3) *N=65*
Race, no (%)			
White/Caucasian	28 (52.8)	10 (62.5)	38 (55.1)
Hispanic/Latino	8 (15.1)	2 (12.5)	10 (14.5)
Black/African American	2 (3.8)	2 (12.5)	4 (5.8)
Other	9 (17)	6 (37.5)	3 (4.3)
More than One Race	4 (7.5)	0 (0)	4 (5.8)
Primary Insurance, no (%)			
Medicaid	32 (60.4)	6 (37.5)	38 (55.1)
Other	21 (39.6)	10 (62.5)	31(44.9)
Pertinent Baseline Comorbidities, no (%)			
Insomnia	19 (35.8)	5 (31.3)	24 (34.8)
Cardiac abnormality	7 (13.2)	4 (25)	11(15.9)
Arrhythmia	3 (5.7)	0 (0)	3 (4.3)
Hypertension	0 (0)	1 (6.3)	1 (1.4)
Neurologic Impairment, no (%)	37(69.8)	14 (87.5)	51(73.9)

*Methylphenidate (37, 69.8%); Mixed amphetamines (13, 24.5%); Dexmethylphenidate (2, 3.7%); Lisdexamfetamine (1, 1.8%)
† Guanfacine (10, 63%); Atomoxetine (3, 18.8%), Clonidine (3, 18.8%)

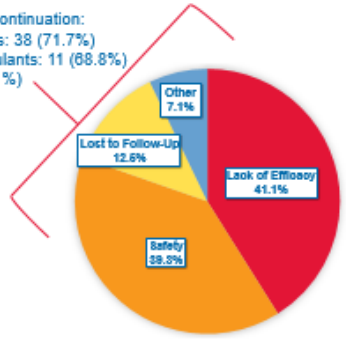
Table 2. Adverse Effects and Related Findings

	Stimulant N=53	Non-Stimulant N=16	All N=69
Initiated on Appetite Stimulant*, no (%)	3 (5.7)	1 (6.3)	4 (5.8)
Median Days to Appetite Stimulant Initiation (IQR)	151 (99, 290)	216	184 (125, 269)
Initiated on Sleep Aid†, no (%)	6 (11.3)	2 (12.5)	8 (11.6)
Median Days to Sleep Aid Initiation (IQR)	55 (28, 62)	170 (166, 173)	62 (42, 170)
Adverse Effects, no (%)			
Sleep Disturbances	5 (9.4)	3 (18.7)	8 (11.6)
Appetite Suppression	3 (5.7)	4 (25)	7 (10.1)
Emotional Lability	7 (13.2)	0 (0)	7 (10.1)
Behavioral Problems	4 (7.5)	0 (0)	4 (5.7)
Self-injurious Behaviors	1 (1.8)	1 (6.2)	2 (2.8)

* Cyproheptadine (4, 100.0%),
† Melatonin (6, 75.0%), Trazodone (1, 12.5%), Diphenhydramine 1 (1, 12.5%)

Figure 2. ADHD Medication Discontinuation Data

Overall Discontinuation:
- Stimulants: 38 (71.7%)
- Non-stimulants: 11 (68.8%)
- All: 49 (71%)



Limitations

- Follow-up period may have been of insufficient duration to capture long term AEs (e.g., suppressed growth or development of neuropsychiatric AEs)[4]
- Discontinuation data includes only index prescription data (subsequent outcomes in those transitioned to new drug are omitted)
- Unable to account for patients who up-titrated appetite suppressants or sleep aids pre-dating ADHD medication initiation

Conclusions

- Most patients initiated on ADHD medications were white, <10 years old and publicly insured
- The high proportion of patients with neurologic impairment was consistent with historical epidemiologic data for CYSHCN[5]
- Emotional lability and behavioral problems occurred more frequently than in non-CYSHCN, but sleep disturbances and appetite suppression did not[6]
- Discontinuation rate was higher than previously observed in CYSHCN[7] and the general population[6]

Implications

- Quality improvement initiatives incorporating pediatric pharmacists at the point of prescribing of ADHD medications in CYSHCN may optimize outcomes
- Pediatric pharmacists may play an integral role in the follow-up care to optimize ADHD management, particularly monitoring and managing adverse effects

Disclosures

The authors have no financial or personal relationships relevant to this presentation.

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Quantification of Safety Outcomes Associated with Attention Deficit Hyperactivity Disorder (ADHD) Medications in Children and Youth with Special Health Care Needs (CYSHCN)
Lionel Sielatchom-Noubissie; Evan Atchley; Lucas Orth, PharmD, BCPPS; Allison Blackmer, PharmD, FCCP, BCPS, BCPPS

Retrospective evaluation of non-tuberculous mycobacteria (NTM) treatment regimens in cystic fibrosis patients

Rebecca M. Wytiaz, PharmD, Kimberly J. Novak, PharmD, BCPS, BCPPS, FPPA

Department of Pharmacy, Nationwide Children's Hospital, Columbus, Ohio

Background

Increasing Incidence of NTM Disease

- Cystic fibrosis (CF) patients vulnerable due to structural lung damage, impaired mucociliary clearance, and inflamed airways[1]
- Incidence in CF patients increased from 1.3% to 12% over 30 years, but true prevalence unknown[1, 2]
- *Mycobacterium avium* complex (MAC) and *Mycobacterium abscessus* complex (MABSC) most common causative species[1]

Need for Standardized NTM Treatment in CF Patients

- Cystic Fibrosis Foundation and Infectious Diseases Society of America/American Thoracic Society guidelines not standardized[1,3]
- Wide variability in NTM treatment exists in CF patients
- Eradication rates and lung function improvement attributed to NTM regimens not reported

Objectives

Primary Objective

- Evaluate NTM regimens at a large CF center including both pediatric and adult programs
- Assess eradication rates and improvement in forced expiratory volume in one second (FEV_1)

Secondary Objectives

- Determine the need for establishment of an optimal NTM treatment strategy for CF patients

Methods

- Retrospective, single-center chart review
- Demographics, NTM regimen duration, pulmonary function, and toxicity information collected
- Descriptive statistics performed

Inclusion Criteria

- Mycobacteria growth on acid fast bacillus (AFB) culture from January 1, 2009 – September 30, 2019
- Received NTM treatment

Exclusion Criteria

- *Mycobacterium tuberculosis* or *Mycobacterium porcinum* growth

Results

Table 1. Study Population

Patient Characteristics	N = 20
Mean age ± SD (years)	30.3 ± 12.0
Mean weight ± SD (kg)	60.1 ±17.8
Males	60%
Pseudomonas aeruginosa colonization	75%
Methicillin-sensitive *Staphylococcus aureus* colonization	45%
Burkholderia cepacia complex colonization	15%
Fungal colonization	30%
Azithromycin therapy prior to positive AFB	37%
Mean +AFB cultures prior to therapy (range)	2.9 (1-6)

Figure 1. NTM Organisms

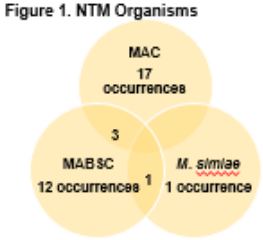

Figure 2. Antimicrobial Use by Indication

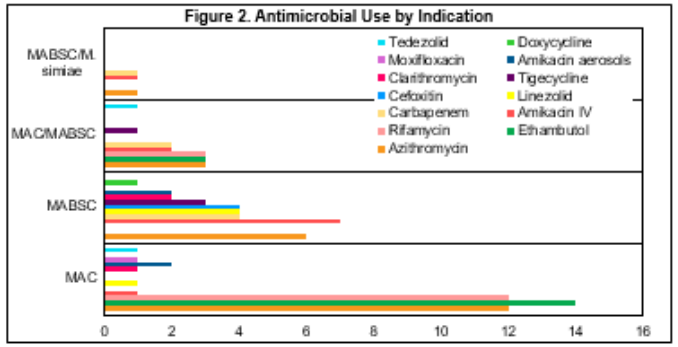

Table 2. NTM Treatment Responses

NTM species	Mean initial FEV_1 (% predicted)	Mean length induction therapy (mo)	Eradication achieved (%)	Median time to eradication (months)	Mean post-therapy FEV_1 (% predicted)
MAC/MABSC	58.3	11.8	66.7	8.8	38.5
MAC	55.6	9.9	75.0	8.3	59.5
MABSC	61.0	6.7	66.7	31.4	61.6
MABSC/*M. simiae*	98.0	18.8	100.0	11.5	N/A

- 59.3% initiated while inpatient
- 74.1% screened for toxicities at initiation
- 22.2% with Infectious Diseases consult
- 59.3% with changes to initial regimen
- 51.9% with recurrent AFB growth during therapy
- 33.3% hearing impairment secondary to amikacin
- 70.8% required fungal therapy
- 77.8% MABSC patients transitioned to continuation phase

Discussion

Evidence for Standardized NTM Treatment in CF

- In MAC, ethambutol, azithromycin, and a rifamycin (most commonly rifabutin) most frequently used
- In MABSC, amikacin IV, azithromycin, a carbapenem (most commonly meropenem) or cefoxitin, and tigecycline, with/without linezolid most often used
- Antimicrobial dosing utilized often higher than guideline recommendations
- Eradication achieved in >60% of all CF patients treated for NTM after an average of 15 months
- FEV_1 modestly increased after treatment for MAC and MABSC
- Over 30% experienced ototoxicity with IV amikacin use, requiring alterations of initial treatment regimen
- Four patients actively receiving therapy

Limitations

- Retrospective chart review study design
- Limited to CF population

Future Directions

- Further studies must be conducted to evaluate eradication in non-CF patients, costs associated with therapy, and an optimal regimen to minimize toxicity

Conclusions

- A high rate of NTM eradication was detected in CF patients at our adult- and pediatric-CF center
- Standardizing treatment regimens for NTM disease could be a valuable opportunity to optimize outcomes

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Disclosures

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

ashp Accredited

Retrospective evaluation of non-tuberculous mycobacteria (NTM) treatment regimens in cystic fibrosis patients
Rebecca M. Wytiaz, PharmD, Kimberly J. Novak, PharmD, BCPS, BCPPS, FPPA

Review of levetiracetam doses utilized in status epilepticus in a pediatric emergency department

Julie Herman, PharmD. Candidate 2021, Daniel Rieck, PharmD., Jenny Steinbrenner, PharmD., BCPPS
Department of Pharmacy, Nationwide Children's Hospital, Columbus, Ohio

Background

- Nationwide Children's Hospital (NCH) utilizes fosphenytoin as its second line agent of choice for status epilepticus (SE)
- Current literature in pediatrics has not shown superiority between fosphenytoin and levetiracetam as a second line agent in SE
- NCH has considered levetiracetam as second line therapy due to improved side effect profile, less interactions, quicker administration and ease of monitoring
- NCH does not have a standard for levetiracetam dosing in SE given the lack of consensus in the literature
- American Epilepsy Society SE guidelines recommend levetiracetam doses of 60 mg/kg (max 4,500mg)

Objectives

Primary

- Evaluate the levetiracetam doses utilized in the emergency department (ED) for SE

Secondary

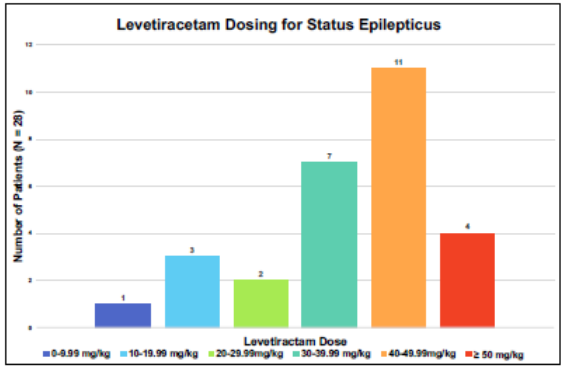
- Evaluate efficacy of initial levetiracetam administration
- Determine use of additional anti-epileptic medications in SE

Methods

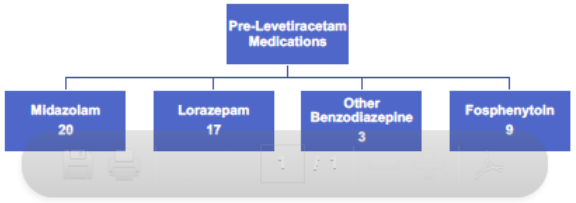
- Single center, retrospective chart review
- Inclusion Criteria: Patients who received intravenous levetiracetam for the treatment of SE in the ED from April 2016 – April 2019
- Patients' electronic medical records were used to obtain baseline demographics, status epilepticus treatment pathway, history of seizures, and home anti-epileptic therapy
- For the purpose of this study, levetiracetam doses of ≥ 40 mg/kg were considered appropriate
- Descriptive statistics were utilized for analysis
- Approved by Investigational Review Board expedited review

Results

Patient Demographics (N = 28)	
Average Age (years)	7
Average Weight (kg)	25.2
History of Seizures n, (%)	22 (78.5)
Home Anti-epileptic n, (%)	18 (64.2)



	Number of Patients (N = 28)	Proportion of Patients	Number with SE Resolution	Proportion with SE Resolution
Dose < 40 mg/kg	13	46.4%	8	61.5%
Dose ≥ 40 mg/kg	15	53.6%	8	53.3%



Discussion

- Overall, 28 patients received levetiracetam for SE in the ED with doses ranging from 9 mg/kg to 52 mg/kg, with an average levetiracetam dose of 36 mg/kg
- Of these patients, dosing was nearly even between appropriate (53.6%) and under-dosed (46.4%)
- For patients appropriately dosed, 53.3% had SE resolution while 61.5% of patients underdosed had SE resolution.
- The average dose of underdosed patients was 25 mg/kg
- All but 1 patient received at least 1 benzodiazepine prior to levetiracetam, and 9 patients received fosphenytoin prior to levetiracetam

Limitations:

- Retrospective study design, small sample size
- Recent literature supports higher dosing than what was defined appropriate in our study
- Exclusion of patients participating in the Established Status Epilepticus Treatment Trial

Conclusions

- Overall there was wide variability in dosing of levetiracetam for SE in the ED. However, dosing was fairly even between appropriate (53.6%) and underdosed (46.4%)
- There was no clear improvement in SE resolution based on utilizing doses of ≥ 40 mg/kg
- A future review utilizing levetiracetam 60 mg/kg for SE may provide better insight for SE resolution

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Review of levetiracetam doses utilized in status epilepticus in a pediatric emergency department
Julie Herman, PharmD. Candidate 2021, Daniel Rieck, PharmD., Jenny Steinbrenner, PharmD., BCPPS

Use of ceftazidime-avibactam for infections caused by multidrug-resistant Gram-negative organisms at a pediatric institution

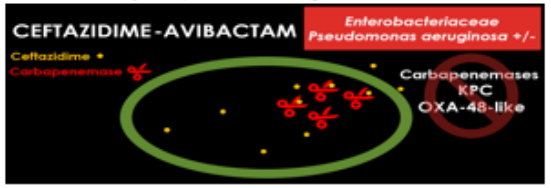
12-095

Ezinwanne Emelue, PharmD; Miranda Nelson PharmD, BCPPS; Christopher McPherson, PharmD, BCPPS; Jason Newland MD, MEd; David Rosen, MD, PhD

St. Louis Children's Hospital, St. Louis, MO

Background

- Ceftazidime-avibactam (CZA) is approved for use in treatment of complicated intra-abdominal infections and urinary tract infections in pediatric patients.
- A paucity of data exists in using CZA for other pediatric infectious disease states caused by carbapenem-resistant organisms.



Objective

Our study aims to describe our institutional experience using CZA for varying infectious diseases caused by carbapenem-resistant organisms.

Methods

- Retrospective chart review of patients who received CZA at St. Louis Children's Hospital between 1/1/2015 and 7/31/2019. Study was approved by the Institutional Review Board of Washington University in St. Louis.
- Inclusion criteria: Any patient who received CZA during our study period.
- Exclusion criteria: Use of CZA for ≤48 hours
- Patients were identified using pharmacy data linked to CZA inpatient orders in electronic medical records.
- Patient demographics, underlying and comorbid disease states, severity of illness, infectious diagnosis, and microbiological data were collected.

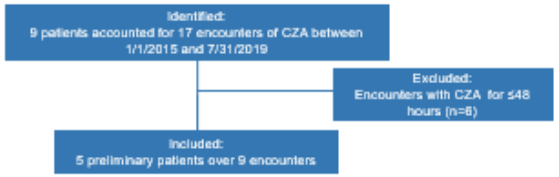


Table 2. Demographics

Patient Demographics	
Age, years*	16 (2 - 20)
Weight, kg*	33.4 (12.7 - 84)
Male	1 (20%)
Female	4 (80%)
Renal Replacement Therapy	1 (20%)
Long-term care facility**	2 (40%)
Prior hospitalization**	5 (100%)
Exposure to Broad Spectrum Antibiotic(s)**	5 (100%)

*Values reported as median (min- max); **Within last 12 months

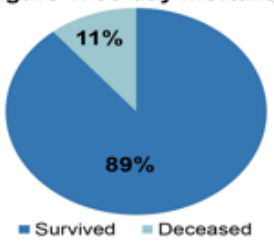
Preliminary Results

Table 1. Patients, Antimicrobial Susceptibility, Ceftazidime- Avibactam Treatment Regimen, and Outcomes

Encounter (Pt. #, Ward)	Comorbid Diseases	Specimen	Organism	Resistance Mechanism	Antimicrobial Susceptibility		CZA Regimen (Dose, Route, Frequency)	Duration (Days)	Time to Microbiologic Clearance (Days)	Clinical Response (Yes or No)
					Susceptible	Non-Susceptible				
1st 1, Non-PICU	Quadriplegic (urinary catheter dependent)	Urine	*Klebsiella pneumoniae*	KPC	C ST, CZA	AMC, AMP, ATM, CIP, FEP, FOX, GEN, IPM, MEM, SXT, TOB, TZP	2,000mg IV q8h	14		Yes
2nd 2,PICU	Cardiogenic shock/ARDS requiring ECMO	Urine	*Citrobacter freundii*	KPC	AMK, CZA, GEN, MVB, MIN, NIT, SXT	AMP, ATM, CAZ, CFZ, CIP, CRO, DOX, ETP, FEP, IMP, MEM, SAM, TOB, TZP	2,000mg IV q8h	7		Yes
3rd 3, PICU	Cystic fibrosis s/p bilateral lung transplant	Urine	*Klebsiella pneumoniae*	KPC	AMK, CZA, CIP, GEN, MVB, NIT	AMP, ATM, CAZ, CDR, CFZ, CRO, CXM, DOX, ETP, FEP, IPM, LEX, MEM, MIN, SAM, SXT, TOB, TZP	50mg/kg/dose IV q8h	9	2	No
		Blood	*Pseudomonas aeruginosa*		ATM, CAZ, CIP, C/T, FEP, GEN, TZP	IPM, MEM				
4th 4, PICU	OEIS with short gut (TPN and trach-vent dependent)	Blood	*Serratia marcescens*	KPC	AMK, CIP, CZA, DOX, MIN, MVB	AMP, ATM, CAZ,CFZ, CRO, FEP, ETP, GEN,IPM, MEM, MIN, SAM, SXT, TZP	50mg/kg/dose IV q8h	47	7	Yes
5th 5, PICU	Spastic CP, severe HIE, epilepsy, trach-vent and GJ tube dependent, global developmental delay, renal insufficiency, incomplete urinary voiding requiring chronic catheter	Urine	*Klebsiella pneumoniae*	KPC	CZA, DOX, MIN, MVB	AMK, AMP, ATM, CAZ, CDR, CFZ,CIP, CRO, CXM, ETP, FEP, GEN, IPM, LEX, MEM, MIN, NIT, SAM, SXT, TOB, TZP	25mg/kg/dose IV q8h	10		Yes
6th 5, PICU		Urine	*Klebsiella pneumoniae*	KPC	AMK, CZA, DOX, MIN, MVB	AMP, ATM, CAZ, CDR, CFZ,CIP, CRO, CXM, ETP, FEP, GEN, IPM, LEX, MEM, NIT, SAM, SXT, TOB, TZP	25mg/kg/dose IV q8h	7		Yes
7th 5, PICU		Blood	*Klebsiella pneumoniae*	KPC	CZA, DOX, MIN, MVB	AMK, AMP, ATM, CAZ, CFZ, CIP, CRO, FEP, ETP, GEN, IPM, MEM, SAM, SXT, TOB, TZP	50mg/kg/dose IV q8h	10	1	Yes
		Urine			AMK, CZA, DOX, MIN, MVB	AMP, ATM, CAZ, CDR, CFZ,CIP, CRO, CXM, ETP, FEP, GEN, IPM, LEX, MEM, NIT, SAM, SXT, TOB, TZP				
8th 5, PICU		Urine	*Klebsiella pneumoniae*	KPC	AMK, CZA, DOX, MIN, MVB	AMP, ATM, CAZ, CDR, CFZ,CIP, CRO, CXM, DOX, ETP, FEP, GEN, IPM, LEX, MEM, NIT, SAM, SXT, TOB, TZP	50mg/kg/dose IV q8h	7		Yes
9th 5, PICU		Urine	*Klebsiella pneumoniae*	KPC	AMK, CZA, DOX, GEN, MVB	AMP, ATM, CAZ, CDR, CFZ,CIP, CRO, CXM, DOX, ETP, FEP, IPM, LEX, MEM, MIN, NIT, SAM, SXT, TOB, TZP	25mg/kg/dose IV q8h	14	10	Yes

AMC indicates amoxicillin- clavulanic acid; ARDS, acute respiratory distress syndrome; AMK, Amikacin; AMP, Ampicillin; ATM, Aztreonam; CAZ, Ceftazidime; CDR, Cefdinir; CFZ, Cefazolin; CIP, Ciprofloxacin; CRO, Ceftriaxone; CP, cerebral palsy; CST, Colistin; CXM, Cefuroxime-axetil; CZA, Ceftazidime-avibactam; C/T, ceftolozane-tazobactam; DOX, Doxycycline; ECMO, extracorporeal membrane oxygenation; ETP, Ertapenem; FEP, Cefepime; FOX, Cefoxitin; GEN, Gentamicin; GJ, gastrojejunostomy; HIE, hypoxic-ischemic encephalopathy; IPM, Imipenem; KPC, *Klebsiella pneumoniae* carbapenemase; LEX, Cephalexin; MEM, Meropenem; MIN, Minocycline; MVB, Meropenem-vaborbactam; NIT, Nitrofurantoin; OEIS, syndrome involving omphalocele, exstrophy of the cloaca, imperforate anus, and spine abnormalities; PICU, Pediatric Intensive Care Unit; SAM, Ampicillin-sulbactam; SXT, Trimethoprim-sulfamethoxazole; TOB, Tobramycin; TZP, Piperacillin-tazobactam.

Figure 1. 30-day mortality



Preliminary Conclusions

- All patients requiring CZA had prior exposure to broad spectrum antibiotics and prior hospital admissions.
- Clinical improvement: 8/9 (88.8%) treatment encounters achieved clinical and symptomatic improvement
- 30 day mortality: 1/9 (11%). Care was redirected during treatment with CZA, and the patient subsequently expired 1 day following CZA discontinuation.
- Discontinuation of CZA due to adverse events was not reported.
- Current results show that CZA has been used in pediatric patients to achieve effective clinical response and microbiological clearance in treating bacteremia and urinary tract infections. More efficacy and safety data is needed for use of CZA in pediatric infectious diseases.

Disclosure

All authors – no financial or personal disclosures to report.

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Use of ceftazidime-avibactam for infections caused by multidrug-resistant Gram-negative organisms at a pediatric institution
Ezinwanne Emelue, PharmD; Miranda Nelson PharmD, BCPPS; Christopher McPherson, PharmD, BCPPS; Jason Newland MD, MEd; David Rosen, MD, PhD