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Mazur, Statner, Dutta, Nathan PC

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Antimicrobial Regimen and Safety of Pediatric Outpatient Treatment in a Physician Office Infusion Center (POIC)

Ramesh V. Nathan, MD, FIDSA[1]; Brian Metzger, MD, MPH[2]; Jorge R. Bernett, MD[3]; Richard C. Prokesch, MD, FACP, FIDSA[4]; Quyen Luu, MD[5]; Kimberly A. Couch, PharmD, MA, FIDSA, FASHP[6]; Claudia P. Schroeder, PharmD, PhD[6]

[1]Mazur, Statner, Dutta, Nathan, PC, Thousand Oaks, CA ; [2]Austin Infectious Disease Consultants, Austin, TX ; [3]Infectious Disease Doctors Medical Group, Walnut Creek, CA; [4]Infectious Disease Associates, Riverdale, GA; [5]Quyen Luu, MD, Macon, GA ; [6]Healix Infusion Therapy, Inc., Sugar Land, TX

Claudia P. Schroeder, PharmD, PhD
Healix Infusion Therapy, Inc.
14140 SW Fwy, Ste. 400
Sugar Land, TX 77478
281-295-4000
cschroeder@healix.net

Abstract, revised

Background: Treatment of pediatric infections through outpatient parenteral antimicrobial therapy (OPAT) is increasing, however data on management and clinical outcomes are limited. This study describes OPAT in pediatric patients (peds) admitted to a POIC including clinical outcomes and safety for a variety of diagnoses.

Methods: A retrospective multi-center (n=20) review was conducted of peds ≤ 18 years (n=64) treated for infection at a POIC from 1-2013 to 12-2014. Data collected included demographics, co-morbidities, cultures, drug regimen, adverse events, emergency department (ED) visit or hospital admissions and clinical outcomes. Clinical success was defined as cure or improvement at end of therapy.

Results: 64 peds were admitted to a POIC over 2 years (yr) for OPAT. Mean age was 16 yr (range 6 -18), with 61% males (n=39). Co-morbidities were infrequent with 32 peds (50%) having none and 16 (25%) having 1. Forty-two peds (66%) had prior hospitalization, whereas 22 peds (34%) had OPAT initiated in the POIC. Most frequent diagnoses included cellulitis with abscess (n=18), osteomyelitis (n=11), complicated intra-abdominal infection (n=9), infectious arthritis (n=6), meningitis (n=5), and postoperative wound infection (n=3). Most common OPAT included cefazolin (n=8), cefepime (n=2), cefotaxime (n=2), ceftriaxone (n=20), daptomycin (n=8), ertapenem (n=9), imipenem/cilastatin (n=3), piperacillin/tazobactam (n=6), and vancomycin (n=10). Seventeen (27%) peds received more than 1 OPAT in combination or sequentially. Mean duration of therapy was 21 days (range 1-56). Six peds (9%) required ED visits, but only 1 (2%) required catheter removal. Adverse events occurred in 19 peds (30%) and included diarrhea (n=5), itching (n=4), thrombocytopenia (n=1), neutropenia (n=1), and drug-induced hepatitis (n=1). Thrombocytopenia, neutropenia, and hepatitis were managed by drug alteration. All patients completed therapy. Clinical success was achieved with 64 peds (100%) with 50 peds (78%) cured and 14 peds (22%) improved.

Conclusion: Based on this 2-year study, use of POIC for the treatment of pediatric infections using various OPAT regimens was a safe and effective option. The incidence of adverse events remained low and treatments were well-tolerated in this population.

Introduction

There is an increasing number of peds being treated through OPAT, however, data on safety and efficacy of intravenous antibiotics in peds are sparse [1-3]. In addition, pediatric OPAT guidelines similar to those available for adults are still needed.

The purpose of this study was to conduct a retrospective, multicenter review of peds admitted to POICs over a 2-year time period with respect to utilization of intravenous antimicrobials, microbiology data, clinical outcomes and associated complications.

Methods

A retrospective review of clinical databases and medical records of 20 Infectious Disease POIC sites was conducted.

Inclusion Criteria

- Patients age ≤ 18 years
- Intravenous therapy received in POIC between January 1, 2013 and December 31, 2014

Data Analysis

- Demographics, co-morbidities, diagnosis, drug therapy, culture results, adverse events, ED visits, hospital admissions, and clinical outcomes at time of therapy completion defined as success rate (%) = "[Cure + Improved/Total number of patients] x 100%":
  - ***Cured***: Clinical signs/symptoms resolved, no additional antimicrobial therapy needed
  - ***Improved***: Partial resolution of clinical signs/symptoms requiring either continued oral antimicrobial therapy and/or follow-up visits
  - ***Failed***: Resistant, worsening, and/or new clinical signs/symptoms at therapy completion
- T-test was applied to determine statistical significance with p≤ 0.05
- Percentages were used for efficacy and safety data

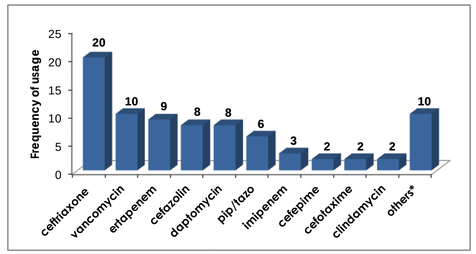
Results

Demographics

Characteristics (n=64)	Results
Gender, No. of peds	
male	39 (61%)
female	25 (39%)
Mean age, years (range)	16 (6 to 18)
Mean BMI* (range)	24 (16.2 - 41.2)
BMI ≥ 30, no. of peds	7 (11%)
Co-morbidities, No. of peds	
asthma	11 (17%)
psychiatric disorder	10 (16%)
gastrointestinal disorder	4 (6%)
sickle cell disease	4 (6%)
cardiovascular disease	2 (3%)
epilepsy	2 (3%)
No. of Co-morbidities per ped	
0	32 (50%)
1	16 (25%)
2	13 (20%)
≥ 3	3 (5%)
Location Prior to OPAT, No. of peds	
home/office	22 (34%)
hospital	42 (66%)

*; Body Mass Index (BMI) >25: overweight, BMI >30: obese

POIC Antimicrobial Usage



*; Others: acyclovir, amikacin, ampicillin/sulbactam, cefoxitin, doxycycline, gentamicin, meropenem, metronidazole, nafcillin, oxacillin (all, n=1). *Abbreviations:* pip/tazo = piperacillin/tazobactam, imipenem = imipenem/cilastatin.

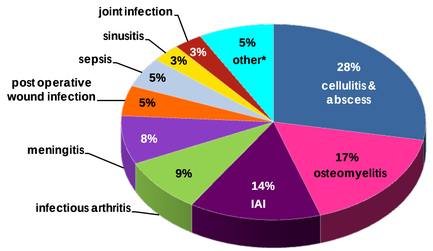
- 64 peds received 80 antimicrobials:
  - ✓ 9 peds (14%) received 2 antimicrobials concomitantly
  - ✓ 8 peds (12%) received ≥ 2 antimicrobials sequentially
- Overall mean length of therapy: 21 days (range, 1 to 56 days). Duration of OPAT was longest for joint infections (33 days) and osteomyelitis (28 days). Shorter durations were used to treat intra-abdominal infections (13 days) and meningitis (9 days)
- All peds had peripherally inserted central catheters (PICC). Drug was delivered using: elastomeric devices (n=59), stationary pumps (n=3), ambulatory pumps (n=2)

Safety

Adverse Event	No. of peds	Intervention	Outcome
diarrhea	5	probiotics, dietary change	resolved
skin rash	3	antihistamines, corticosteroids, drug discontinuation (daptomycin, n=1; ertapenem, n=1)	resolved
fatigue	3	none	resolved
pruritis	3	antihistamines, drug discontinuation (vancomycin, n=1)	resolved
headache	2	analgesics	resolved
nausea	2	proton pump inhibitor	resolved
altered taste	1	drug discontinuation (po rifampin while on vancomycin)	resolved
back pain	1	analgesics	resolved
fever/chills	1	antihistamines, drug discontinuation (vancomycin, n=1)	resolved
elevated LFTs/rash	1	drug discontinuation (nafcillin/clindamycin, n=1)	resolved
drug-induced hepatitis	1	drug discontinuation (po moxifloxacin while on vancomycin/amikacin)	resolved
neutropenia	1	drug discontinuation (cefotaxime/metronidazole, n=1)	resolved
thrombocytopenia	1	drug discontinuation (vancomycin/ceftriaxone, n=1)	resolved

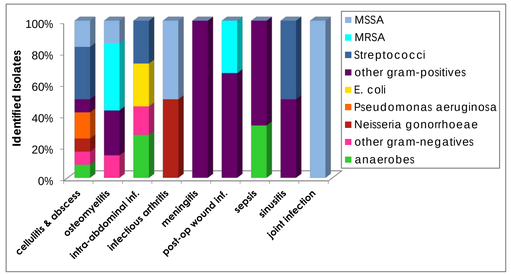
- PICC line was precautionary removed for 1 ped (2%) due to continued fever

Diagnosis



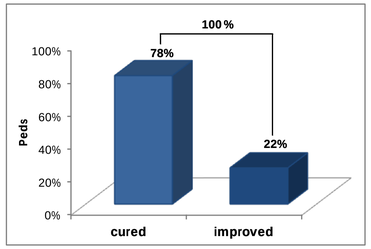
*; Other (n=1, each): empyema, endocarditis, mastoiditis, pancreatitis, urinary tract infection. *Abbreviations: IAI* = intra-abdominal infections

Microbiology by Diagnosis



- Microbiology data were available for 45 pts (70%)
- 11 peds (24%) had polymicrobial cultures
- 12 peds (27%) had no culture growth

Clinical Outcome



- 6 peds (10%) had ED visits including one leading to hospitalization due to drug-related fever (vancomycin)
- 1 ped (2%) had an unplanned hospital admission (day 8)
- 3 peds (5%) had planned inpatient procedures

Discussion

This 2-year retrospective multi-center study using POIC for pediatric OPAT revealed the following results:

- One third of study population received OPAT without prior hospitalization
- Patients had a low number of co-morbidities (average: < 1 co-morbidity per ped)
- Most frequent diagnoses were cellulitis & abscess (28%, n=18), osteomyelitis (17%, n=11), and complicated intra-abdominal infection (14%, n=9)
- Most commonly used antimicrobials were ceftriaxone (31%, n=20), vancomycin (16%, n=10), and ertapenem (14%, n=9)
- Pathogens isolated were 55% gram-positive aerobes, 23% gram-negative aerobes, 9% anaerobes and 17% of peds with polymicrobial cultures
- All drug-related adverse events were successfully managed during OPAT visits.
- No major PICC line complications were experienced (no deep vein thrombosis, no confirmed line infection)
- IV drug discontinuation and/or alterations occurred in 7 peds due to neutropenia (n=1), thrombocytopenia (n=1), elevated LFTs/rash (n=1), rash (n=2), pruritis (n=1) and drug-related fever/chills (n=1)
- Successful clinical outcomes were achieved in all peds with 78% resolved and 22% improved infections and no failure
- Further investigation into the role of OPAT to minimize or avoid hospitalization in the pediatric population is recommended

Conclusion

- Therapeutic success was 100% for peds at POIC
- All adverse events were monitored and managed during POIC visits
- No major catheter complications
- Unplanned hospital admission was minimal (2%)
- POIC was a safe and effective option for the management of a variety of complicated pediatric infections

References

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