Safety and Effectiveness of Outpatient Parenteral Antimicrobial Therapy (OPAT) in the Aged Population

IDWeek™ 2017
#1088

Lucinda J. Van Anglen, PharmD[1]; Richard M. Mandel, MD, FIDSA[2]; Ramesh V. Nathan, MD, FIDSA[3]; Andrew H. Krinsky, MD[4]; Quyen Luu, MD[5]; Alfred E. Bacon III, MD[6]; H. Barry Baker, MD, FACP[7]; Claudia P. Schroeder, PharmD, PhD[1]; Kimberly A. Couch, PharmD, MA, FIDSA, FASHP[1]

[1]Healix Infusion Therapy, Inc., Sugar Land, TX; [2] University of Arizona College of Medicine, Tucson, AZ; [3] Mazur, Statner, Dutta, Nathan, PC, Thousand Oaks, CA; [4] Infectious Diseases Associates, Sarasota, FL; [5] Quyen Luu Central Georgia Infectious Diseases, Macon, GA; [6] Infectious Disease Associates PA, Newark, DE; [7]Infectious Disease Physicians, Miami, FL

Abstract, revised

Background: The aged population (≥75 years) have multiple comorbidities and are at increased risk of adverse events associated with intravenous antimicrobial therapy. Hospitalization (hosp) occurs frequently. This group presents challenges for site of care and reimbursement, which may be met with provision of OPAT through a physician office infusion center (POIC). This setting allows treatment immediately following hosp or directly from the community, thus avoiding hosp. For the aged patient (pt) population, we evaluated safety and effectiveness of OPAT in a POIC.

Methods: Records from 13 POICs were queried for pts ≥75 years receiving OPAT courses from January to July 2016. Data included demographics, therapy, disease characteristics, effectiveness and safety. Effectiveness was assessed as completion of therapy and no unplanned hosp related to the underlying infection. Safety assessment included adverse drug reactions (ADRs), catheter complications (CC) and hosp admissions for causes other than those related to the underlying infection. Risk factors associated with safety were determined using odds ratios (OR).

Results: There were 260 OPAT patient courses provided. Mean age was 81±5 years, 64% male. 51% were treated directly from the community and 49% post hosp. The most common infections were bone and joint (32%), genitourinary (21%), skin and skin structure (20%) and respiratory (12%). OPAT met criteria for effectiveness in 95%, with 247/260 completing therapy and avoiding infection-related hosp. Antimicrobials most frequently used were vancomycin (n=64), ceftriaxone (n=48), cefepime (n=37) and ertapenem (n=32). Median length of OPAT was 14 days (range 1-79). OPAT was assessed as safe in 81% of pts (211/260). 49 pts reported ≥1 safety events including ADRs (40; 15%), CC (6; 2.3%), and hosp (13; 5%). 9 hosp pts completed OPAT following discharge. Most common ADRs were diarrhea (n=9), fatigue (n=9) and nausea (n=10) with 4 hosp for serious ADRs. All CCs resolved and there were no mortalities. Significant risk factors associated with safety events were drug allergies (OR=2.47, CI=1.31-4.65, p=0.005), ≥3 comorbidities (OR=3.92, CI=1.16-13.23, p=0.027), and hypertension (OR=2.19, CI=1.04-4.64 p=0.039).

Conclusion: Provision of OPAT through a POIC demonstrated to be exceptionally safe and effective in the aged population.

Background

The aged population is at increased risk for experiencing ADRs or therapy complications due to physiological changes affecting drug metabolism and clearance, multiple comorbidities and medications [1]. This can result in more frequent and prolonged hosp of elderly pts [2]. OPAT has been shown to be effective and safe for the treatment of infections using intravenous (IV) antimicrobials over a prolonged period of time [3]. However, studies assessing safety in elderly receiving IV therapy in an outpatient setting are limited with even less data available for pts ≥75 years of age. A study conducted in Spain reported comparable rates of ADRs and CCs in OPAT pts of both ≥ and <65 years of age, however, observed higher rates of hosp readmissions due to worsening disease [4].

The aim of this study was to evaluate safety and effectiveness of OPAT in the aged population (pts ≥75 years of age) receiving IV antimicrobials through an Infectious Disease (ID) POIC.

Methods

A retrospective review of medical records was conducted of all pts 75 years and older receiving OPAT for any infection between 01/01/2016 and 06/30/2016 across 13 ID-POICs. The cohort was defined as each pt course of OPAT within a 7-day period, in case a pt received more than one course during the study period. The primary goal of this study was to assess safety and effectiveness of OPAT provided through POICs using the following criteria:

Safety was defined as any ADR(s) occurring during OPAT, CC or hosp admission unrelated to the underlying infection.

Effectiveness was defined as completion of OPAT and no hosp admission related to the underlying infection during OPAT.

Other variables collected included demographics (age, gender, co-morbidities, Charlson co-morbidity index, location prior to OPAT, length of prior hosp stay), infection diagnosis, antimicrobial usage, risk factors and continuation of OPAT following hosp discharge.

Descriptive statistics (mean±SD, percentages) were used for demographics, antimicrobial usage and ADR rate. The ADR rate (%) by antimicrobial was calculated as no. of pt courses with ADR divided by no. of total courses x 100%. Risk factors associated with any safety event were determined using the Altman method including OR and 95% confidence interval (CI) with p-values ≤0.05 defined as statistically significant [5].

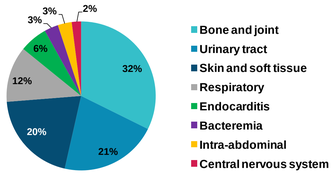
Study Cohort

- Over a 6-month study period, 260 OPAT courses were identified in 236 pts.

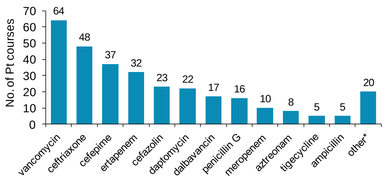
Demographics

Characteristics (n=260)	Results
Age, mean years ± SD	81 ± 5
Gender, male	150 (58%)
Common co-morbidities, no. of pt courses	
Hypertension	175 (67%)
Cardiovascular disease	143 (55%)
Known drug allergy	102 (39%)
Dyslipidemia	87 (33%)
Diabetes mellitus	82 (32%)
Obesity	66 (25%)
No. of co-morbidities per OPAT course	
0	3 (1%)
≥3	212 (82%)
≥5	112 (43%)
Charlson index, mean ± SD	5.6 ± 1.6
Location prior to OPAT, no. of pt courses	
Community	133 (51%)
Hospital	127 (49%)
Mean length of hospital stay, days ± SD	6 ± 3

Infection Diagnosis



Antimicrobial Usage

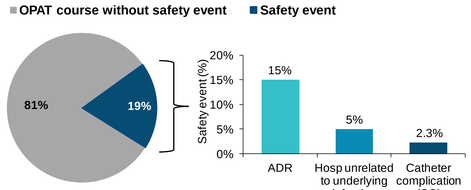


- Overall median length of OPAT was 14 days (range 1-79 days)
- 29 of 260 pt courses (11%) received concomitant IV therapies

*other: amikacin (n=2), ceftazidime (n=2), gentamicin (n=2), imipenem/ cilastatin (n=2), micafungin (n=2), oxacillin (n=2), piperacillin/tazobactam (n=2), acyclovir (n=1), cefoxitin (n=1), ceftolozane/tazobactam (n=1), clindamycin (n=1), fluconazole (n=1), metronidazole (n=1)

Safety

Summary of Safety Events

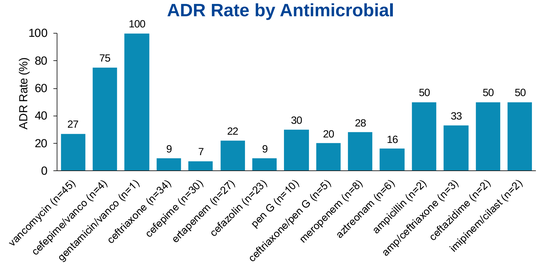


Characterization of ADRs

Organ System	Frequency	Median Onset (therapy day)	Outcome
Gastrointestinal	**33%**		
Nausea & vomiting	10	7	
Diarrhea	9	3	
Loss of appetite	2	9	
C. difficile diarrhea	1	3	
Dermatological	**19%**		
Rash	6	21	OPAT discont. (n=1)
Pruritus	4	8	
Candidiasis	3	8	
Hematological	**6%**		
Anemia	2	10	hosp (n=1)
Blood dyscrasias	1	5	
Thrombocytopenia	1	10	
Cardiovascular	**8%**		
Edema	2	6	
Hypotension	2	10	
Bradycardia	1	22	
Neurological	**6%**		
Dizziness	2	9	
Altered mental status	1	13	hosp (n=1)
Headache	1	5	
Renal	**4%**		
Renal insufficiency	3	12	hosp (n=1)
Immunological	**4%**		
Hypersensitivity	2	5	hosp/OPAT discont. (n=1)
Anaphylaxis	1	1	hosp/OPAT discont. (n=1)
Others	**19%**		
Fatigue/weakness	9	7	hosp (n=2), OPAT discont. (n=3)
Pyrexia	2	22	
Metallic taste	2	6	

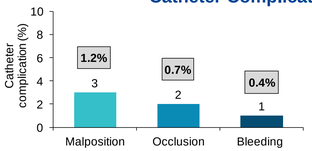
- A total of 67 ADRs were reported in 40 pt courses

ADR Rate by Antimicrobial



Safety, cont.

Catheter Complications



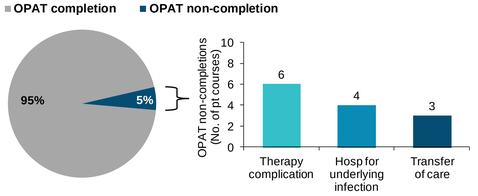
- A total of 6 CCs (2.3%) were reported in 260 pt courses
- All CCs resolved

Potential Predictors

Risk factor	OR	95% CI	P Value
Significant			
Known drug allergies (n=27)	2.47	1.31 to 4.65	0.005
Co-morbidities ≥3 (n=46)	3.92	1.16 to 13.23	0.027
Hypertension (n=39)	2.19	1.04 to 4.64	0.039
Non-significant			
Vancomycin use (n=17)	1.85	0.94 to 3.63	0.072
Concomitant IV antimicrobials (n=9)	2.15	0.91 to 5.06	0.080
Co-morbidities ≥5 (n=25)	1.48	0.79 to 2.77	0.214

Effectiveness

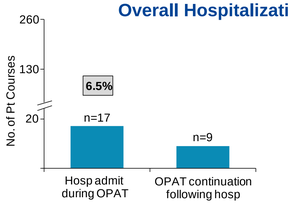
Summary of Effectiveness



247 of 260 pt courses (95%) successfully completed OPAT, 13 (5%) did not due to:

- therapy-related complications (5 ADRs, 1 OPAT-unrelated)
- hosp for underlying infection (4)
- transfer to other care settings (3)

Overall Hospitalization Rate



- 260 pt courses had 17 hosp due to safety events (13) and underlying infections (4)
- 9 of 17 pts (53%) continued OPAT following hosp discharge

Discussion

This geriatric study determined safety and effectiveness of OPAT in pts ≥75 years treated at ID POICs over a 6-month time period:

- 260 OPAT courses were identified in 236 pts (mean age: 81±5 years, mean Charlson index: 5.6±1.6) from 13 ID POICs
- 51% of elderly pts avoided hospitalization prior to OPAT
- Most common diagnosis were bone and joint (32%), urinary tract (21%), and skin and skin structure infections (20%)
- Most frequent antimicrobials were vancomycin (21%), ceftriaxone (16%), cefepime (12%) and ertapenem (10%) including 11% concomitant therapies. Median length of OPAT was 14 days.
- **Safety:** OPAT was safe in 81%, whereas 19% (n=49) experienced ≥1 safety event including 15% ADRs, 5% hosp and 2.3% CCs. ADRs were frequently related to gastrointestinal (33%) and dermatological (19%) symptoms. All but 6 pts continued OPAT following interventions. The majority of ADRs were reported with the use of vancomycin.
- Risk factors significantly attributing to safety events were prior drug allergies [OR 2.47 (95% CI 1.31-4.65), p=0.005], ≥3 co-morbidities [OR 3.92 (95% CI 1.16-13.23), p=0.027], and hypertension [OR 2.19 (95% CI 1.04-4.64), p=0.039]
- **Effectiveness:** OPAT was effective in 95% pts. Reasons for non-completion included therapy complications (2.3%), hosp for underlying disease (1.5%) and transfer of care (1.2%)
- Hospitalizations occurred during OPAT in 17 of 260 pt courses (6.5%). Of those, 9 pts (53%) successfully completed OPAT following hospital discharge
- Limitations of this study include the retrospective nature and the absence of comparator groups

Conclusion

OPAT provided to aged pts ≥75 years through ID POICs was safe in 81% of pts. In addition, 95% of pts completed their OPAT course with no hosp underlying to infection meeting the criteria for effectiveness. Hospitalizations were low with an overall rate of 6.5% and no mortalities.

This study supports the safe and effective provision of OPAT to the aged population through an ID POIC.

References

1. McLean AJ and Le Couteur DG. Aging, biology, and geriatric clinical pharmacology. *Pharmacol Rev* 56:163-84, 2004
2. Nagamine M, et al. Trends in elderly hospitalizations, 1997-2004. Healthcare Cost and Utilization Project. *Statistical Brief* #14, 2006
3. Tice A, et al. Practice guidelines for outpatient antimicrobial therapy. IDSA guideline. *Clin Infect Dis* 38:1651-72, 2004
4. Mujal A, et al. Safety and effectiveness of outpatient parenteral antimicrobial therapy in older people. *J Antimicrob Chemother* 71(5):1402-7, 2016
5. Altman DG: Practical statistics for medical research. *Chapman & Hall/CRC* edition 1, London 1991