

# Complications Associated with Pediatric Outpatient Parenteral Vancomycin Therapy

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## Introduction

- Pediatric use of intravenous (IV) vancomycin in the outpatient setting has increased due to the advent of peripherally inserted central catheters and the availability of skilled outpatient nursing services.
- The most common complications in adults treated with vancomycin outpatient parenteral antimicrobial therapy (OPAT) are rash and nephrotoxicity.
- Rates and types of complications associated with pediatric outpatient vancomycin therapy are unknown.

## Objectives

For subjects receiving vancomycin in our OPAT Program at Boston Children's Hospital:

1. Describe baseline patient characteristics.
2. Describe the most common complications encountered during therapy.
3. Determine predictors of unplanned outcomes due to complications.

## Methods

- Retrospective study of subjects discharged on vancomycin OPAT and followed by the infectious diseases service from August 2008 through April 2016.
- Demographic and clinical data related to the OPAT course were collected via chart review.
- Complications were categorized as:
  - Antimicrobial-related
  - IV-access-related
- Complication-associated outcomes evaluated included:
  - Premature antimicrobial discontinuation/change (PAD)
  - Unplanned healthcare visit (UHV)
  - Unplanned readmission (UR)

## Methods

| Antimicrobial-related complications   | IV-access-related complications   |
|---|---|
| Laboratory abnormalities:<br>WBC: <4 K/uL<br>ANC: <1 K/uL<br>Platelets: <150 K/uL<br>Eosinophil count: >0.5 K/uL<br>AST/ALT: >80 units/L<br>Creatinine: age dependent<br>Antimicrobial level outside planned range<br>Drug rash<br>Nausea/vomiting/diarrhea<br>Fever<br>Anaphylaxis<br><i>Clostridium difficile</i> infection | Inability to draw back<br>Inability to infuse<br>Insertion site reaction<br>Catheter-associated bloodstream infection<br>Line site infection<br>Line migration<br>Equipment malfunction |

Unplanned event secondary to complication

| Outcomes                                |                            |                       |
|---|----------------------------|-----------------------|
| Premature antimicrobial discontinuation | Unplanned healthcare visit | Unplanned readmission |

Abbreviations: WBC=white blood cell count, ANC=absolute neutrophil count, AST=aspartate transaminase, ALT=alanine transaminase

### Statistical Analysis:

- Bivariate regression analyses identified demographic and clinical characteristics that were significantly associated with each of two outcomes: PAD and a combined outcome of UHV and/or UR.
- Multivariate regression models used risk factors significant on bivariate analyses, forcing in certain clinically significant variables (pathogen, diagnosis, concomitant antimicrobial use, duration of vancomycin).

## Results

Table 1: Demographic and clinical characteristics

|  | N=150 (%)        |
|--|------------------|
| <b>Age (years; median/IQR)</b>                   | 13.4 (7.7, 17.2) |
| <b>Male gender</b>                               | 88 (58.7)        |
| <b>Diagnosis</b>                                 |                  |
| Musculoskeletal infections                       | 49 (32.7)        |
| Central nervous system infections <sup>1</sup>   | 47 (31.3)        |
| Endocarditis                                     | 28 (18.7)        |
| Surgery-associated infections                    | 15 (10)          |
| Other  | 11 (7.3)         |
| <b>Pathogen if isolated<sup>2</sup></b>          |                  |
| Aerobe, gram positive                            |                  |
| <i>Staphylococcus aureus</i>                     | 45 (30)          |
| CoNS   | 23 (25.3)        |
| Anaerobe   |                  |
| <i>Propionibacterium</i> spp.                    | 21 (14.0)        |
| <b>Surgery</b>                                   |                  |
| None   | 37 (24.3)        |
| Any  | 114 (75.7)       |
| <b>Type of IV access</b>                         |                  |
| PICC   | 146 (97.3)       |
| Other  | 4 (2.7)          |
| <b>Duration of vancomycin (days; median/IQR)</b> | 27.5 (18, 43)    |
| <b>Concomitant antimicrobial(s)</b>              |                  |
| No   | 67 (44.7)        |
| Yes  | 83 (55.3)        |
| <b>Outcomes</b>                                  |                  |
| PAD  | 41 (27.3)        |
| UHV  | 65 (44)          |
| UR   | 39 (26)          |
| Combined outcome (UHV and/or UR)                 | 73 (48.6)        |

<sup>1</sup>Including complications arising from otitis media, mastoiditis and sinusitis

<sup>2</sup>More than one pathogen isolated in some cases

Abbreviations:

IQR: interquartile range, CoNS: coagulase-negative *Staphylococcus* spp., IV: intravenous, PICC: peripherally inserted central catheter, PAD: premature antimicrobial discontinuation, UHV: unplanned healthcare visit, UR: unplanned readmission

Table 2. Breakdown of outcomes by complications

|                               | Premature antimicrobial discontinuation n(%) | Unplanned healthcare visit/readmission n(%) |
|-------------------------------|--|---|
| Leukopenia/Neutropenia        | 7 (13.5)                                     | 6 (6.1)                                     |
| Elevated eosinophil count     | 2 (3.8)                                      | 2 (2)                                       |
| Hepatic transaminitis         | 0 (0)  | 3 (3.1)                                     |
| Elevated creatinine           | 6 (11.5)                                     | 2 (2)                                       |
| Abnormal antimicrobial levels | 9 (17.3)                                     | 2 (2)                                       |
| IV-access-related             | 6 (11.5)                                     | 29 (29.6)                                   |
| Drug rash                     | 10 (19.2)                                    | 8 (8.2)                                     |
| Nausea/vomiting               | 2 (3.8)                                      | 6 (6.1)                                     |
| Fever                         | 7 (13.5)                                     | 23 (23.5)                                   |
| Other                         | 3 (5.8)                                      | 17 (17.3)                                   |

Table 3. Risk factors for outcomes (multivariable regression models)

| Outcome             | Risk factor                                   | Odds ratio (95% CI)                    | P value               |
|---------------------|---|--|-----------------------|
| PAD <sup>1</sup>    |   |  |                       |
|                     | Any complication                              | CoNS <sup>2</sup>                      | 3.199 (1.006, 10.172) |
| Rash                |   |  |                       |
|                     | Duration of therapy (for each additional day) |  | .939 (.884, .998)     |
| UHV/UR <sup>3</sup> |   |  |                       |
|                     | IV-access-related                             | Diagnosis of endocarditis <sup>4</sup> | .182 (.037, .895)     |

<sup>1</sup> Adjusted for pathogen, use of concomitant antimicrobials, duration of vancomycin

<sup>2</sup> Comparison group=*Staphylococcus aureus*

<sup>3</sup> Adjusted for diagnosis, use of concomitant antimicrobials, duration of vancomycin

<sup>4</sup> Comparison group=musculoskeletal infections

## Conclusions

1. Complications are common in vancomycin OPAT, with a third of children experiencing PAD and slightly less than half experiencing UHV and/or UR.
2. Drug rash is the most common cause of PAD, and intravenous access-related problems are the most common cause of UHV/UR. In contrast with findings in adults, nephrotoxicity (defined by elevated creatinine) occurred infrequently.
3. Transition to oral antimicrobial alternatives should be encouraged when possible.
4. Future research should explore the role of CoNS in complications and compare the outcomes of alternative antimicrobials to vancomycin to determine the most safe outpatient therapy

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