# Achieving Vancomycin Serum Level Goals in the Home Infusion Setting: Continuous versus Intermittent Infusion

**Eric Slayton, PharmD[1] | Bryan Eskew, PharmD, MS[2]**

1. Coram CVS Specialty Infusion Services, Marietta, GA 2.Coram CVS Specialty Infusion Services, Albany, NY

## Introduction

Vancomycin remains a mainstay of therapy for various indications, particularly those caused by methicillin resistant Staphylococcus aureus (MRSA). Vancomycin therapy success is dependent upon achieving targeted AUC, with serum trough levels often set as surrogate goals. Dose adjustments are required when targeted serum trough levels are not achieved, as sub-therapeutic levels jeopardize the success of therapy, and supra-therapeutic levels increase the risk of side effects. Dose adjustments become complicated, however, when serum levels are not drawn appropriately with respect to the patients' dosing schedules. In such scenarios, practitioners are then forced to use complex pharmacokinetic equations, electronic dosing platforms, or professional discretion to determine how to adjust the vancomycin dose according to the mistimed blood draw.

Although vancomycin is most commonly administered via intermittent infusion (II), administration by continuous infusion (CI) has been found to offer distinct advantages while achieving similar cure rates[1-3]. With CI, there are no trough levels to obtain; rather, the concentration at steady-state (Css) is used to measure vancomycin in serum. As a result, there are no requirements for blood draws with respect to timing once steady state has been achieved[4]. Additionally, studies have demonstrated that patients given CI vancomycin rather than II vancomycin achieve target serum goals more quickly[5], are managed on simpler dosing and monitoring protocols[6], and have lower risk of nephrotoxicity[7-9]. However, as most existing literature concerning the use of CI vancomycin focuses specifically on the inpatient setting, it is uncertain whether or not CI vancomycin offers the same advantages in the home infusion setting.

## Purpose

The purpose of this study as to determine if patients who received CI vancomycin were more likely to attain serum vancomycin goal levels than patients who received II vancomycin, while also assessing for correlation between infusion method and completion of therapy as ordered.

## Methods

In retrospective analysis, 27 patients were identified who received vancomycin therapy between July 1, 2018 and June 30, 2019. 15 received II vancomycin, and 12 received CI vancomycin. Patient monitoring data, including vancomycin serum levels, were collected for each patient. The goal serum vancomycin level was documented for each patient. The manner of therapy completion was also recorded, whether it was as ordered by the prescriber or discontinued due to side effects, inability to maintain goal serum levels, or any other reason. Proportional analysis with z-score was performed for comparisons between both groups' attainment of goal serum levels, completion of therapy as ordered, and mistimed levels. Mean data for change in serum creatinine (sCr) was tested for normality with the Kolmogorov-Smirnov Test and subsequently analyzed with the Mann-Whitney U Test. All significance levels were set at $p \leq 0.05$.

## Results

### Table 1: Characteristics of Study Population

| Patient Demographics and Characteristics | | |
|---|---|---|
| | Continuous Infusion (n=12) | Intermittent Infusion (n=15) |
| Age (average) | 48 | 64 |
| Gender | | |
| - Male | 7 (58%) | 5 (33%) |
| - Female | 5 (42%) | 10 (66%) |
| Indication | | |
| - osteomyelitis | 6 (50%) | 8 (53%) |
| - skin infection | 4 (33%) | 5 (33%) |
| - endocarditis | 1 (8%) | 2 (13%) |
| - pneumonia | 1 (8%) | 0 (0%) |
| Concomitant antibiotics | | |
| - rifampin | 1 (8%) | 2 (13%) |
| - piperacillin/tazobactam | 1 (8%) | 1 (7%) |
| - levofloxacin | 1 (8%) | 1 (7%) |
| - ceftriaxone | 3 (25%) | 3 (20%) |
| - none (monotherapy) | 6 (50%) | 8 (53%) |
| Concomitant NSAIDs | 1 (8%) | 1 (7%) |
| Concomitant diuretics | 2 (16%) | 3 (20%) |
| Diabetes | 3 (25%) | 6 (40%) |

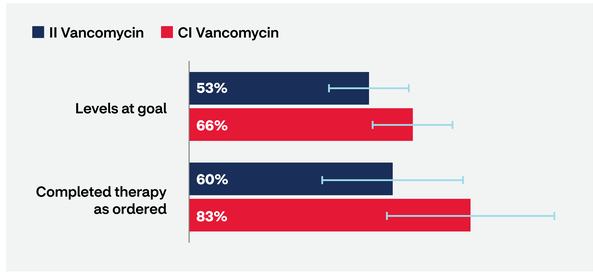
*Abbreviations: NSAIDs – non-steroidal anti-inflammatory medications*

### Table 2: Characteristics of Therapy

| Therapy Characteristics | | | |
|---|---|---|---|
| | Continuous Infusion (n=12) | Intermittent Infusion (n=15) | p value |
| Total vancomycin days | 419 | 503 | |
| - Length of Therapy (days, average) | 35 | 34 | |
| - Levels drawn | 61 (1.0)* | 73 (1.0)* | |
| - Mistimed levels | 0 (0)* | 12 (0.17)* | 0.0009 |
| - Dose adjustments | 17 (0.28)* | 31 (0.43)* | 0.08 |

**Representative of event per 7 days of vancomycin therapy across all patients per infusion method*

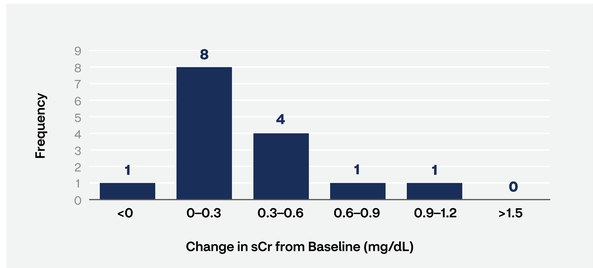
### Figure 1: Goal Attainment




*Error bars represent standard error.*

**Figure 1:** Percentage of serum vancomycin levels measured at goal and percentage of orders completed with originally intended duration of therapy.

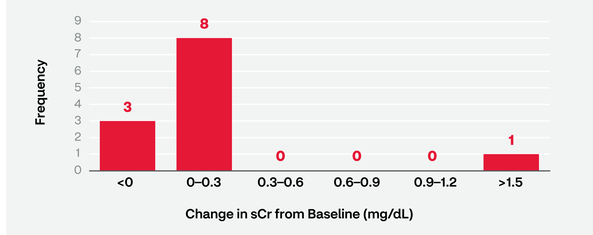
### Figure 2: Change in Serum Creatinine – II Vancomycin




*Abbreviations: II – intermittent infusion, sCr – serum creatinine*

**Figure 2:** Serum creatinine change from start of care to completion of therapy among patients who received II vancomycin.

### Figure 3: Change in Serum Creatinine – CI Vancomycin




*Abbreviations: CI – continuous infusion, sCr – serum creatinine*

**Figure 3:** Serum creatinine change from start of care to completion of therapy among patients who received CI vancomycin.

### Table 3: Outcomes of Interest

| Outcomes | | | |
|---|---|---|---|
| | Continuous Infusion (n=12) | Intermittent Infusion (n=15) | p value |
| Levels at goal | 66% | 53% | 0.07 |
| Completed Therapy as Ordered | 83% | 60% | 0.09 |
| Median Change in sCr (mg/dL) | 0.03 | 0.26 | 0.0027* |

**U = 28*
*Significance was set at $p \leq 0.05$.*
*Abbreviations: sCr – serum creatinine*

## Conclusions and Clinical Implications

- **The change in sCr was significantly greater in patients who received vancomycin by II, as is consistent with findings from previous studies[7-9]**
- **While not statistically significant, goal levels were obtained more frequently when vancomycin was administered as CI, and patients who received vancomycin by CI were able to complete their therapy as ordered with greater consistency**
- **The occurrence of mistimed levels was significantly greater in patients who received II vancomycin, with 12 such events overall in 8 out of 15 patients, compared to no such events in CI vancomycin patients**
- **This study was limited by small sample size and inconsistency in average age among study groups**
- **Additional studies may be warranted to explore patient satisfaction between infusion methods, cost burden of nursing and medical equipment, and differences in reported side effects**

### References

1. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm*. 2020.
2. Vuagnat A, Stern R, Lotthe A et al. High dose vancomycin for osteomyelitis: continuous vs. intermittent infusion. *J Clin Pharm Ther*. 2004; 29(4):351-357.
3. Verrall AJ, Llorin R, Tam VH et al. Efficacy of continuous infusion of vancomycin for the outpatient treatment of methicillin-resistant *Staphylococcus aureus* infections. *J Antimicrob Chemother*. 2012; 67(12):2970-2973.
4. Waineo MF, Kuhn TC, Brown DL. The pharmacokinetic/pharmacodynamic rationale for administering vancomycin via continuous infusion. *J Clin Pharm Ther*. 2015;40(3):259-265.
5. Byl B, Jacobs F, Wallemacq P, et al. Vancomycin penetration of uninfected pleural fluid exudate after continuous or intermittent infusion. *Antimicrob Agents Chemother*. 2003;47(6):2015-2017.
6. Wysocki M, Delatour F, Faurisson F, et al. Continuous versus intermittent infusion of vancomycin in severe Staphylococcal infections: prospective multicenter randomized study. *Antimicrob Agents Chemother*. 2001;45(9):2460-2467.
7. Cataldo MA, Tacconelli E, Grilli E, Pea F, Petrosillo N. Continuous versus intermittent infusion of vancomycin for the treatment of Gram-positive infections: systematic review and meta-analysis. *J Antimicrob Chemother*. 2012;67(1):17-24.
8. Saugel B, Nowack MC, Hapfelmeier A, et al. Continuous intravenous administration of vancomycin in medical intensive care unit patients. *J Crit Care*. 2013;28(1):9-13.
9. Ingram PR, Lye DC, Fisher DA, Goh WP, Tam VH. Nephrotoxicity of continuous versus intermittent infusion of vancomycin in outpatient parenteral antimicrobial therapy. *Int J Antimicrob Agents*. 2009; 34(6):570-574.