CASE REPORT

# Oral Absorption of Enteral Vancomycin in a Child with *Clostridium difficile* Colitis and Renal Impairment

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Vancomycin is a glycopeptide antibiotic that is used by the enteral route for the treatment of *Clostridium difficile* infections and is not thought to be absorbed into the systemic circulation. We report on a 2-year-old, 12.5-kg patient with confirmed *C difficile* colitis and renal insufficiency that was treated with 125 mg of enteral vancomycin (10 mg/kg); the patient developed measurable systemic concentrations as high as 17.8 mg/L. However, as the patient's colitis began to improve, the serial vancomycin concentrations reflected little to no continued absorption of vancomycin. A review of the literature regarding this rare phenomenon is discussed.

**INDEX TERMS** *Clostridium difficile,* pharmacokinetics, vancomycin

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## INTRODUCTION

Vancomycin is a glycopeptide antibiotic that is used by the enteral route for the treatment of *Clostridium difficile* infections. Because of its pharmacokinetics, including the size of the molecule, vancomycin is not thought to be absorbed into the systemic circulation in a normally functioning bowel. We report the case of a pediatric patient with severe bowel inflammation and renal insufficiency who exhibited systemic absorption and accumulation of vancomycin following oral administration.

## CASE PRESENTATION

Our patient was a 2-year-old female; she had been diagnosed with hepatoblastoma, which was being treated with cisplatin, vincristine, 5-fluorouracil, and doxorubicin. The patient's past medical history was significant for renal insufficiency that intermittently required continuous renal replacement therapy (CRRT). The patient presented to the pediatric intensive care unit for typhlitis and persistent febrile neutropenia. During hospitalization, she was treated with broad-spectrum agents, including piperacillin/tazobactam, linezolid, micafungin, metronidazole, and monthly pentamidine. The patient had also received cefepime and meropenem approximately 2 weeks prior to this regimen.

Thirteen days into her stay in the intensive care unit, she was tested for *C difficile* toxin due to persistent fevers, gastrointestinal bleeding, and abdominal computed tomography findings consistent with intestinal edema and inflammation. This test was positive for *C difficile* toxin, and vancomycin 125 mg/dose (10 mg/kg) was begun and given via nasogastric tube every 6 hours. Enteral vancomycin was chosen, since the patient developed the infection while receiving intravenous metronidazole. At the time vancomycin was initiated, the patient was on CRRT, serum creatinine was 1.02 mg/dL, and blood urea nitrogen was 30 mg/dL.

On day 3 of enteral vancomycin, concern was expressed that the combination of a significantly inflamed gastrointestinal tract and renal insufficiency could lead to systemic absorption and accumulation of vancomycin. A vancomycin concentration of 12.5 mg/L was measured approximately 6 hours after the previous dose of vancomycin and approximately 18 hours after discontinuation of CRRT therapy. At this time, it was decided to maintain the current dosing of vancomycin.

Another vancomycin concentration was drawn 48 hours later (after an additional 8 doses) and

**Table.** Vancomycin Dosing and Serum Concentrations

| Day | Time | Vancomycin Serum Concentration (mg/L) | Time Since Last Dose (hr) | Serum Creatinine (mg/dL) | Event |
|---|---|---|---|---|---|
| 1 | 13:38 | | | 1.76 | Vancomycin 125 mg NG every 6 hr initiated |
| 2 | 17:35 | | | 1.96 | CRRT stopped |
| 3 | 11:45 | 12.5 | 6 | 2.15 | |
| 5 | 12:00 | 17.8 | 6.75 | 0.7 | |
| 5 | 20:30 | 16.2 | 15.25 | | |
| 5 | 21:24 | | | | Vancomycin changed to 62.5 mg NG every 12 hr |
| 6 | 9:20 | 15.9 | 12 | 1.17 | |
| 6 | 23:00 | 14.1 | 1.5 | | |
| 7 | 8:55 | 13 | 11.5 | 0.8 | |
| 7 | 10:00 | | | | Vancomycin changed to 62.5 mg NG every 6 hr |
| 7 | 12:50 | 12.1 | 3 | | |
| 7 | 20:00 | 11.2 | 2 | | |
| 8 | 5:00 | 10 | 4.75 | 1.02 | |
| 8 | 12:50 | | | | Vancomycin increased to 125 mg NG every 6 hr |
| 9 | 12:20 | 8.5 | 6 | 1.05 | |
| 9 | 14:10 | 8.4 | 1.5 | | |
| 9 | 17:55 | | | | Vancomycin NG was discontinued |
| 12 | 12:00 | 2.2 | 66 | 1.88 | |

*CRRT, continuous renal replacement therapy; NG, nasogastric*

was 17.8 mg/L. This demonstrated continued absorption of the enteral vancomycin. The nursing staff confirmed that the patient had not been receiving any form of intravenous vancomycin since 14 days prior to the start of enteral therapy.

To limit the amount of vancomycin absorbed into the systemic circulation, the dose of vancomycin was decreased and the dosing interval was extended. The Table depicts the vancomycin administration times and doses along with the serial vancomycin concentrations. As the patient's colitis began to improve, serial concentrations demonstrated little to no continued absorption of vancomycin. As the dose and frequency of orally administered vancomycin increased, there was no evidence of systemic absorption of the vancomycin; the serum concentrations continued to trend downward. The patient's condition improved, and vancomycin was eventually discontinued on day 9 of therapy.

## DISCUSSION

This report discusses a pediatric patient with significant enteral absorption of oral vancomycin in the presence of impaired gastrointestinal wall integrity with concomitant renal insufficiency. While normally vancomycin's pharmacokinetics limit oral absorption,[1] it has been noted that systemic absorption is possible after enteral administration. In 1983, Thompson et al[2] presented a 14-year-old female patient with renal insufficiency and pseudomembranous colitis that was treated with oral vancomycin 250 mg every 6 hours. This patient eventually attained serum concentrations between 13.5 and 34 mg/L, along with an unexplained encephalopathy that rapidly resolved upon initiation of hemodialysis with reduction in serum vancomycin concentrations to 24 mcg/mL.[2] While the accumulation of enteral vancomycin is most often reported in patients

with renal insufficiency,[3,4] it has also been noted to occur in patients with pseudomembranous colitis without compromised renal function.[5,6] This is most often attributed to compromised intestinal epithelium allowing for increased drug absorption.

According to the available data, there may be a relationship between the dose of oral vancomycin administered and serum concentration attained. Matzke et al[7] demonstrated that there was a significant linear relationship between daily dose and serum concentration obtained in patients with moderate to severe renal impairment who were being treated with escalating doses (125 mg to 500 mg every 6 hours) of oral vancomycin for antibiotic-associated colitis.[7] This dose-response relationship is supported by other studies that included patients with varying degrees of renal insufficiency who were treated with 125 mg of vancomycin every 6 hours and were unable to reliably produce detectable serum concentrations of vancomycin.[8,9] While it is possible that the use of 125 mg of vancomycin every 6 hours in our patient was a sufficient dose to lead to therapeutic serum concentrations, this is not supported by the fact that the serum concentrations did not rise in response to increasing the dose from 62.5 mg to the original dose of 125 mg on day 8 of therapy. This lack of rise of serum concentrations may indicate that the patient's colitis was resolving and the integrity of the gastrointestinal epithelium was returning.

## CONCLUSION

This paper reports on a 2-year-old patient with significant systemic absorption of enteral vancomycin in the presence of *C difficile* colitis and renal insufficiency. Practitioners should be cognizant of this rare phenomenon and be careful in choosing those patients who may benefit from monitoring of serum vancomycin concentrations.

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**ABBREVIATIONS** *C difficile, Clostridium difficile*; CRRT, continuous renal replacement therapy

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## REFERENCES

1. *Vancocin* [package insert]. Zanesville, OH: Cardinal Health; 2011.
2. Thompson CM, Long SS, Gilligan PH, et al. Absorption of oral vancomycin - possible associated toxicity. *Int J Pediatr Nephrol*. 1983;4(1):1-4.
3. Spitzer PG, Eliopoulos GM. Systemic absorption of enteral vancomycin in a patient with pseudomembranous colitis. *Ann Intern Med*. 1984;100(4):533-534.
4. Yamazaki S, Nakamura H, Yamagata S, et al. Unexpected serum level of vancomycin after oral administration in a patient with severe colitis and renal insufficiency. *Int J Clin Pharmacol Ther*. 2009;47(11):701-706.
5. Aradhyula S, Manian FA, Hafidh SA, et al. Significant absorption of oral vancomycin in a patient with *Clostridium difficile* colitis and normal renal function. *South Med J.* 2006;99(5):518-520.
6. Bergeron L, Boucher FD. Possible red-man syndrome associated with systemic absorption of oral vancomycin in a child with normal renal function. *Ann Pharmacother.* 1994;28(5):581-584.
7. Matzke GR, Halstenson CE, Olson PL, et al. Systemic absorption of oral vancomycin in patients with renal insufficiency and antibiotic-associated colitis. *Am J Kidney Dis.* 1987;9(5):422-425.
8. Rao S, Kupfer Y, Pagala M, et al. Systemic absorption of oral vancomycin in patients with *Clostridium difficile* infection. *Scand J Infect Dis*. 2011;43(5):386-388.
9. Armstrong CJ, Wilson TS. Systemic absorption of vancomycin. *J Clin Pathol.* 1995;48(7):689.