

The Effect of Intravenous Vancomycin in the Reduction of the Incidence of *Clostridium difficile* Colitis

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Abstract

The gastrointestinal tract infection known as Pseudomembranous Colitis caused by bacteria *Clostridium difficile* (*C. difficile*). The massive overpopulation of *C. difficile* can result in conditions ranging from mildly debilitating antibiotic associated diarrhoea to life-threatening toxic mega-colon. This study will examine whether having Vancomycin as part of the antibiotic treatment regimen for various types of sepsis leads to a decreased incidence of antibiotic induced pseudomembranous colitis formation when compared to other antibiotic treatments alone without Vancomycin.

Keywords: Colitis; Bacteria; Antibiotics; Vancomycin

Introduction

Pseudomembranous Colitis is a gastrointestinal tract infection caused by the bacteria *Clostridium difficile* (*C. difficile*). *Clostridium difficile* is frequently found in the normal colon, but pathologic overgrowth of *C. difficile* often occurs following destruction of the normal intestinal flora by antibiotics. This massive overpopulation of *C. difficile* can result in conditions ranging from mildly debilitating antibiotic associated diarrhoea to life-threatening toxic mega-colon.

A large multihospital study of over 10,000 patients found that the adjusted mean cost and length of stay of patients with *Clostridium difficile* infections was nearly double that of matched control patients (\$55,769 vs \$28,609; 21.1 vs 10.0 days) [1]. Another recent study calculated that a hospital with 4.1 cases of *C. difficile* infection per 100,000 patient discharges would incur a cost of greater than or equal to \$3.2 million dollars [2]. It also found the annual US economic burden of *C. difficile* infections to be greater than or equal to \$496 million dollars [2]. Preventing these infections would result in lowering both the economic burden, possibly decrease the growing rate of drug resistant bacteria, and decrease the morbidity and mortality associated with pseudomembranous colitis.

Although commonly thought to be exclusively eliminated by the kidney, a small scale study of 54 patients found that intravenous Vancomycin may be partially excreted in the bile. They found detectable levels of Vancomycin (3.3 to 94.8 µg/mL) in the stools of 92.5% of patients five days after initiation of intravenous Vancomycin administered at a rate of 1 gram every 12 hours [3]. However, only one patient's stool sample contained Vancomycin levels when it was administered at a rate of one gram every 24 hours.

This study will examine whether having Vancomycin as part of the antibiotic treatment regimen for various types of sepsis leads to a decreased incidence of antibiotic induced pseudomembranous colitis

formation when compared to other antibiotic treatments alone without Vancomycin.

Methods

This retrospective study selected for patients over the age of 18 admitted to our 410-bed community teaching hospital between January 1, 2011 and November 30, 2013 who presented without diarrhoea and with the diagnosis of sepsis and other infections. The inclusion criteria was all adults, admitted to the hospital during a three year period with the diagnosis of sepsis, severe sepsis, pneumonia, UTI, cellulitis, acute exacerbation of COPD, and septic shock. Excluded were patients diagnosed with diarrhoea on admission, with a recent history of *C. difficile* in the previous 30 days, or had treatment with flagyl or oral vancomycin at admission. We defined IV vancomycin treatment as administration of greater than 24 hours. Therefore, patients that had vancomycin ordered less than 24 hours prior to *C. difficile* testing were categorized as non-vancomycin treatment.

The rate of *C-difficile Pseudomembranous colitis* and the number of patients receiving IV vancomycin was calculated by frequencies and percent. The association between the proportion of patients receiving IV vancomycin and the proportion of patients having *P. colitis* was analysed by Chi-square analysis. The magnitude of effect was calculated by Odds Ratio with significance set at $p < 0.05$. An incidence of new infection among patients on antibiotics was estimated to be 5% and approximately 70 patients per day are hospitalized with sepsis. In order to determine that a 25% effect difference is significant, 700 sepsis patients were calculated to achieve a power of 85%.

Results

There were 4128 patients meeting inclusion criteria. Two patients were removed due to a lack of documentation. The final study sample included 4126 patients. There were 2387 (57.9%) females and 1736 (42.1%) males. The mean age was 64.7 yr (SD=17.7; range=18–102).

Comorbid conditions included COPD: 1598 (38.7%), CKD: 609 (14.8%), DM: 1258 (30.5%) and malignancies: 1506 (36.5%). The majority met criteria with 4123 (99.9%) having neither Flagyl or diarrhoea and none of these tested positive for *C. difficile*.

Forty six patients (1.1%) tested positive for *C. difficile* during their hospital stay. Prior medical history of *C. difficile* was noted in 120 (2.9%) patients. In regards to treatment, 1455 (35.3%) had been given Vancomycin. There were 4 patients missing data on Vancomycin and were excluded from the analysis. The breakdown of other antibiotics given is provided in Table 1. The most common other antibiotic was the class of beta lactams (2171 or 52.6%) and Quinolones (1690 or 59.0%).

Other Antibiotics	Frequency	Percent
0	586	14.2
1	1821	44.1
2	1038	25.2
3	456	11.1
4	167	4.0
5	41	1.0
6	6	0.1
7	4	0.1
Total	4119	99.8*

*Seven missing antibiotic information.

Table 1: Breakdown of other antibiotics.

Endpoints

There was no significant difference in *C. difficile* rates between patients receiving vancomycin and those not receiving it (OR=0.83, CI: 0.4–1.6) (p=0.64). The group with no vancomycin had slightly higher incidence of *C. difficile* colitis but the difference was not statistically significant (Table 2).

	C. difficile # (%)
Vancomycin (n=1454)	14 (1.0)
No vancomycin (n=2667)	31 (1.2)

Table 2: Outcome Rates by Treatment Group.

The lower incidence in the vancomycin group was more pronounced in the male population but did not reach the statistical significance as well (Table 3). Age differed by Vancomycin group (63.6 Vs 65.2, p=0.01) and by *C. difficile* group (70.8 Vs 64.6, p=0.02). After adjusting for age and gender differences, the association between vancomycin use and *C. difficile* result remained non-significant (OR=1.2, CI: 0.6–2.2, p=0.63).

C. difficile # (%)	Males (n=1734)	Females (n=2387)	p-value
Vancomycin	5/730 (0.7)	9/724 (1.2)	0.32
No vancomycin	12/1004 (1.2)	19/1663 (1.1)	0.98
p-value	0.33	0.84	
OR (CI)	0.57 (0.2–1.6)	1.1 (0.5–2.4)	0.83 (0.4-1.6)

Table 3: Effect of Gender on Outcome Rates by Treatment Group.

Discussion

To our knowledge no studies have looked at the protective effect of intravenous vancomycin against the development of *C. difficile* colitis. The current study sought to test the hypothesis whether treatment with intravenous Vancomycin leads to a decreased incidence of pseudomembranous colitis formation when compared to other antibiotics alone. The findings demonstrated that the difference in the reduction of *C. difficile* colitis with the treatment of intravenous vancomycin was minimal and not statistically significant.

Pathologic overgrowth of *Clostridium difficile* (*C. difficile*) is a major concern for hospital admission patient management [1]. Because *C. difficile* is found within the normal flora of the colon and antibiotic treatment is common during admission, patients are susceptible to *C. difficile* related conditions ranging from mildly debilitating antibiotic-associated diarrhoea to life-threatening toxic [3]. Methods to reduce the incidence of *C. difficile* colitis are continually sought. Unfortunately based on this retrospective study, treatment with intravenous vancomycin which is very common in hospitalized patient does not result in a reduction of *C. difficile* colitis that is statistically significant.

In summary, this retrospect study has failed to show a beneficial/protective effect of the treatment with intravenous vancomycin in the reduction of the incidence of antibiotics induced pseudo membranous colitis caused by *C. difficile* bacteria.

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