Bile Acid Concentrations in Healthy Volunteers Receiving Oral Omadacycline or Vancomycin

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BACKGROUND

- Antibiotic exposure has significant and long-lasting impacts on gut microbiota resulting in a loss of colonization resistance against pathogens such as *Clostridioides difficile*[1]
- Antibiotic-induced gut microbiota changes lead to reduced conversion of primary to secondary bile acids[2]
- Reduced levels of secondary bile acids increase the likelihood of *C. difficile* spore germination and *C. difficile* infection (CDI) recurrence[2]
- Omadacycline, a tetracycline analog, has potent *in vitro* activity against *C. diffcile* but its effect on the host microbiome has not been studied in-depth in humans[3,4]
- This study was designed to assess changes in bile acid concentrations in healthy volunteers given oral omadacycline compared to vancomycin, the most common antibiotic used to treat CDI

OBJECTIVE

- To compare primary and secondary bile acid concentrations in healthy volunteers receiving oral omadacycline or vancomycin

METHODS

Inclusion criteria

- Healthy subjects aged 18 to 45 years
- No significant past medical history
- No antibiotic use in the 28 days prior to enrollment

Study design

- Subjects were randomized to receive 10 days of oral omadacycline (450 mg daily on days 1 and 2 followed by 300 mg daily) or oral vancomycin (125 mg four times daily)

Sample collection

- Stool samples were collected at baseline, during antibiotic days, at end of therapy, and at follow-up visits

Bile acid analysis

- Targeted bile acids were extracted and quantified via liquid chromatography-mass spectrometry (LC-MS)
- For this analysis, stool samples collected at the end of therapy were analyzed for primary and secondary bile acids

RESULTS

Table 1. Patient Demographics

Characteristics	Subjects (n=16)
Age, mean (±SD), y	26.1 ± 5
Male, no. (%)	10 (63%)
Race/ethnicity, no. (%) White, non-Hispanic Black, non-Hispanic Asian	 6 (38%) 4 (25%) 6 (38%)
Weight, mean (±SD), kg	70.5 ± 17
Body mass index, mean (±SD), kg/m^2	23.5 ± 3.9
Dietary habits, no. (%) Omnivore Vegetarian	 14 (88%) 2 (13%)

Figure 1. Primary Bile Acid Concentrations

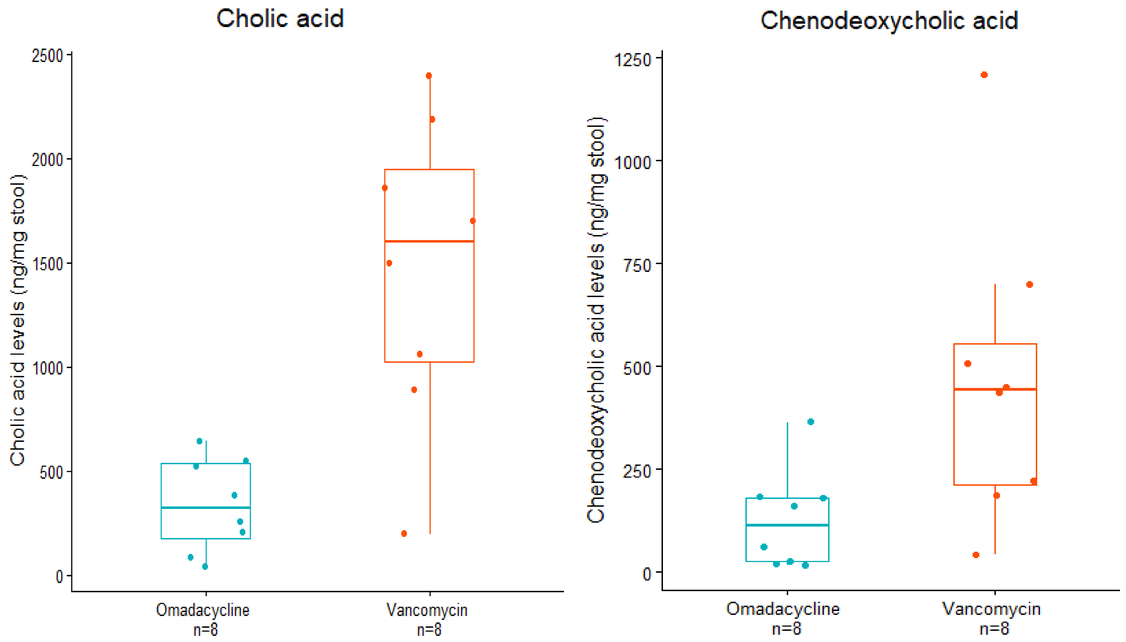
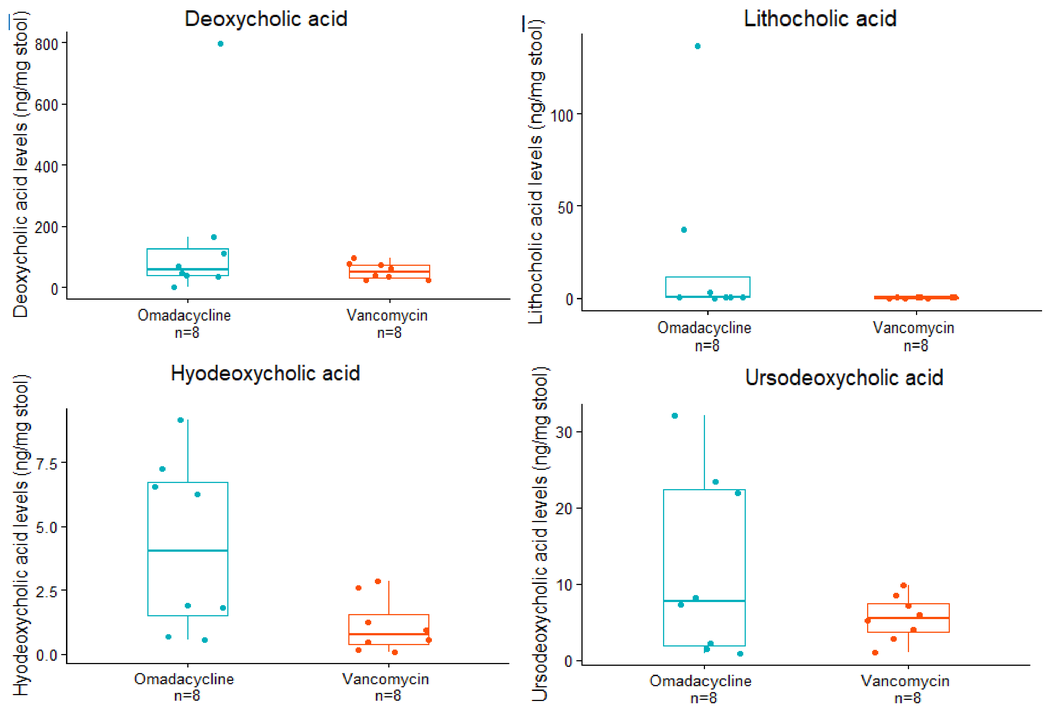


Figure 2. Secondary Bile Acid Concentrations



CONCLUSIONS

- Omadacycline preserved bile acid homeostasis in the gut to a higher extent than vancomycin, suggesting reduced microbiome dysbiosis
- The results of this study along with omadacycline's potent *in vitro C. difficile* activity and availability as an oral and IV formulation support future research for the treatment of CDI

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