






Concise Communication

Clostridioides difficile infection following dental antibiotic prescriptions in a cohort of US veterans

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Abstract

Among 108 (0.05% of cohort) US veterans with a *Clostridioides difficile* infection (CDI) within 30 days of a dental antibiotic prescription, 80% of patients received guideline-discordant antibiotics. Half had chronic gastrointestinal illness potentially exacerbating their CDI risk. More efforts are needed to improve antibiotic stewardship.

(Received 19 August 2021; accepted 14 December 2021; electronically published 21 February 2022)

Dentists prescribe ~6% of all antibiotics in the Veterans' Health Administration (VHA), and they are the leading prescribers of clindamycin.^{1,2} Concern about dental antibiotic overprescribing has increased due to the rise in *Clostridioides difficile* infection (CDI) and antimicrobial-resistant infections.³ The American Heart Association (AHA) in collaboration with the American Dental Association (ADA) developed guidelines in 2007 for the prevention of infective endocarditis that stated that antibiotic prophylaxis was indicated for patients with a history of certain cardiac conditions undergoing gingival manipulation.⁴ The 2019 ADA clinical practice guidelines (CPG) for the treatment of acute oral infections advised that antibiotics were only appropriate for acute apical abscesses.⁵ Data on the association between dentist-prescribed antibiotics and CDI are scarce. Here, we describe our analysis of Veterans who received an antibiotic prescription from a VA dentist and subsequently developed CDI within 30 days. We evaluated guideline concordance with either the ADA-CPG or infective endocarditis prophylaxis guideline.

Methods

Patients with dental antibiotic prescriptions within 7 days of a dental visit were identified from 2015 through 2019 using data from the VA Corporate Data Warehouse (CDW). Patients with a positive CDI test within 30 days after the dental encounter were included. CDI positivity was determined by standard practice at

each facility. Chart reviews using the electronic health record were conducted to collect information on dental procedures, oral infection, documented reasons for prescription, antibiotic type, dosage and duration, and antibiotic allergies. CDI information included date of testing, CDI treatment, and recurrent CDI (defined as 2 positive CDI test within 90 days). Chronic gastrointestinal (GI) conditions (including gastroesophageal reflux disease (GERD), diverticulitis, gastric cancers, irritable bowel syndrome, inflammatory bowel syndrome, and ulcerative colitis) described in patients' electronic health record were identified. Prescriptions for proton pump inhibitors (PPIs) or H2 receptor antagonists (H2RAs), were similarly identified within a year prior to the dental visit.

The VA CDW was used to obtain patient demographics and to determine the presence of a cardiac condition and/or gingival manipulation during the dental visit. Evidence of prosthetic joint replacement in the previous 2 years or an immunocompromising condition (defined as a diagnosis of cancer, HIV/AIDS, rheumatoid arthritis, and/or solid-organ transplantation) were collected. Cardiac conditions (including but not limited to history of valve replacement, infective endocarditis, or cardiac transplant) were defined using both *International Classification of Disease, Ninth and Tenth Revisions* (ICD-9/-10) and current procedural terminology (CPT) codes according to the AHA/ADA guidelines.⁴ Gingival manipulation was defined using the codes for dental procedures and nomenclature (ie, CDT) based on previous work.^{6,7} Pulpitis, periodontitis, and acute apical abscess were defined according to ICD-9/-10 codes.² Guideline-concordant antibiotic prescriptions were defined as the presence of qualifying pre-existing cardiac condition necessitating dental prophylaxis in patients undergoing gingival manipulation or a diagnosis of acute apical abscess.^{4,5}

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Cite this article: Wilson GM, et al. (2023). *Clostridioides difficile* infection following dental antibiotic prescriptions in a cohort of US veterans. *Infection Control & Hospital Epidemiology*, 44: 494–496, <https://doi.org/10.1017/ice.2021.516>



Prescriptions not meeting this definition were considered guideline discordant. Descriptive statistics were calculated using SAS version 9.4 software (SAS Institute, Cary, NC). This study was approved by the Hines VA Institutional Review Board.

Results

Between 2015 and 2019, 212,763 patients had an antibiotic prescribed by a VA dentist within 7 days of a dental encounter. Of these, 108 patients (0.05%) had a positive diagnostic test for *C. difficile* within 30 days and were included in the cohort. The included patients were predominantly male (95 of 108) and of white race (82 of 108) (Table 1). The average patient age was 60.8 years (SD, 13.9). Also, 59.3% had a chronic GI condition, and 34.3% reported GERD. Furthermore, 50% of the study population was prescribed either a PPI or an H2RA. Also, 26.7% of the cohort had prosthetic joints and 4.8% had an immunocompromising condition.

Gingival manipulation occurred at 76.9% of the visits, and 19.4% of the cohort had a preexisting cardiac condition. Gingival manipulation included tooth extraction (34.3%) and implant placement surgery (12.1%), which may require postprocedural prophylaxis. Moreover, 31.5% of the cohort had an acute oral infection; the most common was pulpitis (29.6%), followed by acute apical abscess (2.8%), and periodontitis (1.9%). Also, 14 patients (12.9%) received antibiotics concordant with the infective endocarditis prophylaxis guidelines. Furthermore, 8 patients (7.4%) were prescribed antibiotics in accordance with the ADA-CPG guidelines, which were published during the final year of the study period. Most of this cohort (79.7%) received antibiotics that were discordant with both guidelines. Of those with discordant antibiotic prescriptions, 24.4% had prosthetic joints and 4.6% were immunocompromised.

The most prescribed antibiotic was amoxicillin (54.6%), followed by clindamycin (38.9%). For amoxicillin and clindamycin, >80% of patients were prescribed for ≥ 4 days. Furthermore, 28% of the cohort had a documented penicillin allergy, accounting for 89% of those who received clindamycin. The most frequently documented reasons for prescribing were presence of a local infection (37.9%), postprocedural prophylaxis (23.2%), and premedicating patients with cardiac conditions (11.1%). However, 17.6% had no documentation from the dentist explaining the indication for the prescription.

CDI was considered recurrent for 6.5% of the cohort. Furthermore, 91.7% were experiencing GI symptoms indicative of active CDI at the time of their stool test. CDI was treated primarily with oral vancomycin (49.1%), followed by metronidazole (45.4%). Only 5 patients (4.6%) were not prescribed any antibiotics, and 1 patient (0.9%) was prescribed probiotics.

Discussion

In this descriptive analysis of 108 VA patients with CDI following dentist-prescribed antibiotics, 80% of prescribed antibiotics were guideline discordant. Postprocedural prophylaxis was the documented reason for prescription in 23.2% of patients. A 2021 Cochrane review of antibiotic prophylaxis for tooth extractions reported that prophylaxis may reduce the risk of postsurgical infection and dry sockets. However, the numbers of patients needed to treat were high for each condition (19 for postsurgical infection and 46 for dry socket).⁸

In this study, a significant percentage of those patients with a documented penicillin allergy were prescribed clindamycin

Table 1. Demographic and Medical Characteristics of Veterans with CDI After an Antibiotic Prescribed by a Dentist (N = 108)

Characteristic	Total No. (%) ^a
Age, mean y (SD)	60.8 (13.9)
Sex, male	95 (87.9)
Race/Ethnicity	
White	82 (75.9)
Black	13 (12.0)
Asian	1 (0.9)
Latine	3 (2.8)
Native American	1 (0.9)
Native Hawaiian/Pacific Islander	1 (0.9)
Multiracial	3 (2.8)
Missing	4 (3.7)
Gastrointestinal condition	
None	44 (40.7)
Gastroesophageal reflux disease	37 (34.3)
Diverticulitis	8 (7.4)
Other ^b	19 (17.6)
Use of gastric acid reducer (PPI or H2RA)	54 (50.0)
Region	
Northeast	21 (19.4)
Midwest	26 (27.1)
West	32 (29.6)
South	29 (26.9)
AHA/ADA IE prophylaxis guidelines criteria	
Cardiac condition	21 (19.4)
Gingival manipulation	83 (76.9)
Oral infections	
Pulpitis	32 (29.6)
Periodontitis	2 (1.9)
Acute apical abscess	3 (2.8)
Dental prescriptions (all patients n = 108)	
Amoxicillin	59 (54.6)
Clindamycin	42 (38.9)
Other ^c	7 (6.5)
Dental prescriptions (penicillin allergy n = 29)	
Amoxicillin	1 (3.4)
Clindamycin	26 (89.6)
Other ^c	2 (6.9)

Note. SD, standard deviation; PPI, proton pump inhibitor; H2RA, H2 receptor antagonist; AHA/ADA, American Heart Association/American Diabetes Association.

^aNo. (%) unless otherwise indicated.

^bOther gastrointestinal conditions include but are not limited to colon cancer, gastroparesis, and neurogenic bowel.

^cOther antibiotics include amoxicillin/clavulanic, penicillin, and azithromycin.

(89%). A 2021 statement published by the AHA is now recommending against the use of clindamycin for persons that are allergic to penicillin because of the documented increased risk of adverse events, namely CDI.⁹ The results of our analysis support the conclusions made by the AHA.

Most patients in this study had a history of chronic GI illness (59.3%), and 34.3% had GERD, which is higher than the estimated GERD prevalence rate in the VA population (8%–28%).^{10,11} The literature has shown an increased risk of CDI for persons with GERD, which is hypothesized to be related to dysbiosis associated with the disease.¹² Furthermore, 50% of the study population received a PPI or H2RA, which has also been linked to an increased risk of CDI and a synergistic risk of CDI when combined with antibiotic use.¹³ Although our current results do not causally link the dental antibiotics to the subsequent CDI event, the antibiotics prescribed by a dentist represent an additional exposure.

This study had several limitations. These results may not be generalizable because antibiotics prescribed by non-VA prescribers were not captured. Veterans are predominately older males and may not be representative of the US population. Data were collected before the publication of the ADA-CPG, so provider adherence to those guidelines is not reflected.

In conclusion, although the number of included patients is small, most patients included in this analysis were prescribed an antibiotic discordant with current guidelines governing use of antibiotics in a dental setting. Many of the included participants had known risk factors for CDI, such as chronic GI illnesses that further increased their risk of CDI. We recommend increased vigilance by dentists to antimicrobial stewardship, awareness of identified risk factors, and an increased adherence to guidelines.

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