No Impact of Probiotics to Reduce Clostridium difficile Infection in Hospitalized Patients: A Real-world Experience

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We assessed the effectiveness of a Lactobacillus probiotic on rates of health care facility–onset Clostridium difficile infection (HO-CDI) in patients receiving antibiotics. A total of 1576 patients were evaluated. There was no difference in the HO-CDI incidence between those who received probiotics and those who did not (1.8% vs 0.9%; \(P = .16\)).

Keywords. Clostridium difficile infection; hospitalized patients; probiotics.

Hospitals participating in the Centers for Medicare and Medicaid Services report health care facility–onset Clostridium difficile infection (HO-CDI) data to the National Healthcare Safety Network. The Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America endorse recommendations to assist acute care hospitals in implementing and prioritizing their CDI prevention efforts [1]. Although probiotics is not an endorsed strategy, a recent supplement published in Clinical Infectious Diseases recommends probiotics, specifically the combination of Lactobacillus acidophilus CL1285, Lactobacillus casei LBC80R, and Lactobacillus rhamnosus CLR2 (Bio-K+), as an intervention to reduce CDI rates [2]. Based on data presented, our institution added Bio-K+ to the formulary, and as part of a “bundle” to reduce risk of HO-CDI, Bio-K+ was recommended to be administered to patients on antibiotic therapy identified as high risk for CDI. In addition, education was provided to medical staff regarding the availability of Bio-K+, and physicians could choose to administer Bio-K+ at their discretion. This study evaluated the rates of HO-CDI for a 6-month time period among patients who received intravenous (IV) antibiotics plus Bio-K+ vs IV antibiotics alone.

METHODS

This was a retrospective cohort study conducted at a 400-bed community hospital in La Jolla, California. All hospitalized patients treated with IV antibiotics during the study period were evaluated for enrollment. Adult patients (age ≥18 years) who received at least 1 dose of antibiotics and had a length of stay >3 days were included. Patients were excluded if CDI was community onset (diagnosed within 3 days of hospital admission) or if they received cefazolin or cefoxitin for surgical prophylaxis only. The primary outcome was the incidence of HO-CDI in patients who received IV antibiotics plus probiotics vs IV antibiotics alone. Bio-K+ was the only probiotic used was and was prescribed at the discretion of the attending physician.

Baseline demographic data, length of stay, age, Charlson Comorbidity Index, billed grams of antibiotics, acid inhibitor use, number of days on probiotics, intensive care unit (ICU) stay, and in-house mortality were evaluated. Patients were identified to have received IV antibiotics if they received at least 1 dose of the following: vancomycin, ciprofloxacin, levofloxacin, ceftriaxone, ceftazidime, cefepime, piperacillin/tazobactam, imipenem/cilastatin, meropenem, ertapenem, cefazolin, or cefoxitin. Patients were considered to be on probiotics before the onset of HO-CDI if any doses of Bio-K+ were recorded before the date of Clostridium difficile toxin testing. The study was approved by the Scripps Institutional Review Board.

Descriptive statistics were used to analyze demographic data across the 2 cohorts. Continuous outcomes were analyzed by 2-tailed Student \(t\) test, and dichotomous data were analyzed by the Pearson \(\chi^2\) test or Fisher exact test (for cell size <5). All statistical analyses were performed using R: A Language and Environment for Statistical Computing, version 3.0.1 (Vienna, Austria) [3].

RESULTS

Between March 29, 2016, and September 30, 2016, a total of 1576 patients treated with IV antibiotics were evaluated, of whom 649 received antibiotics plus probiotics and 927 were treated with antibiotics alone. Both groups were similar with respect to age (65.8 vs 67.2 years; \(P = .15\)), ICU stay (48.4% vs 49.2%; \(P = .32\)), and in-house mortality (8.2% vs 6.8%; \(P = .32\)). HO-CDI occurred in 11 of 649 patients who received antibiotics plus probiotics and in 8 of 927 patients treated with antibiotics alone (1.8% vs 0.9%, respectively; \(P = .16\)) (Table 1). The median duration of probiotic treatment was 8.1 days. Patients in the probiotic group had a longer length of stay, a higher

Received 27 April 2018; editorial decision 1 August 2018; accepted 22 August 2018.
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DOI: 10.1093/ofid/ofy192

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In this study, we evaluated HO-CDI and did not differentiate with no benefit on treatment or prevention of recurrence [6]. These studies demonstrated very large effect sizes of Lactobacillus-containing probiotics compared with placebo (95% [7] and 75% [8] reduction in CDI, respectively) in populations with very high first-episode CDI prevalence rates (23.8% [7] and 40% [8], respectively). Our results and CDI prevalence are more consistent with the PLACIDE study and population [9]. This large, multicenter, double-blinded, placebo-controlled trial randomized hospitalized patients to a probiotic containing 2 strains of Lactobacillus acidophilus and bifidobacteria vs placebo and observed no difference in CDI rates (12 of 1470 patients [0.8%] vs 17 of 1471 patients [1.2%]; \( P = .35 \)). Recent CDI guidelines affirm the need to use caution in applying study results with an abnormally high baseline incidence of CDI and conclude that there are insufficient data at this time to recommend probiotics for primary prevention of CDI outside of clinical trials [1].

Antibiotic use is the most important modifiable risk factor for CDI in acute care hospitals. The Centers for Disease Control estimates that at least 30% of antibiotic use is unnecessary [10]. Based on these findings, our institution removed all probiotics from the hospital formulary and removed all probiotics from the hospital formulary.
from the formulary. Instead, we endorse strong antimicrobial stewardship practices that are shown to be efficacious and caution that probiotics may consume health care resources without adding additional benefit.

Acknowledgments

Prior presentation. This paper was presented at the Infectious Diseases Society of America ID Week Meeting; October 4–8, 2017; San Diego, CA.

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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