Impact of a pharmacist-driven probiotic protocol on *Clostridioides difficile* infection at a community hospital

Purpose: *Clostridioides difficile* (*C. difficile*) is an antibiotic-associated infection with significant morbidity and mortality. The Centers for Disease Control and Prevention (CDC) has identified *C. difficile* as an urgent antibiotic resistance threat resulting in over $1 billion of healthcare costs in 2017. Improving antibiotic usage has been proven to prevent *C. difficile* infections (CDI) while studies examining the efficacy of probiotics for prevention have yielded inconsistent results. In January 2018, Olathe Medical Center implemented a policy allowing pharmacists to order probiotics for patients receiving broad-spectrum antibiotics at high-risk for CDI. The purpose of this study was to compare the occurrence of CDI in patients receiving high-risk antibiotics before and after the implementation of this pharmacist-driven probiotic protocol.

Methods: This was a retrospective cohort study with a primary outcome of CDI within six months of discharge. All patients admitted between March 2015 to March 2016 and March 2018 to March 2019 with an order for a high-risk broad-spectrum antibiotic were included for pre- and post-protocol analysis, respectively. High-risk antibiotics included ceftriaxone, cefepime, piperacillin-tazobactam, ciprofloxacin, levofloxacin, meropenem, or ertapenem. Patients were randomized and examined for eligibility for lactobacillus acidophilus/casei/rhamnosus (Bio-K®) based on hospital protocol and it was documented if the patient received probiotics during admission. A total of 300 patients, 150 patients per group, who met the inclusion and exclusion criteria were analyzed to achieve statistical power. Data from the National Healthcare Safety Network (NHSN) was used to determine if the patient had a documented CDI within six months of discharge. Secondary outcomes included pharmacist adherence to the protocol and occurrence of CDI in patients with a documented penicillin allergy.

Results: There were 7 cases of CDI in pre-protocol group and 4 cases in the post-protocol group (p=0.36) with 5 patients receiving probiotics during admission. Presence of CDI risk factors according to hospital protocol were similar among each group except for a significant decrease in use of acid suppression therapy in the post-protocol group (p=0.02). There were differences in antibiotic usage with a significant decrease in use of levofloxacin (35 v. 16, p=0.003) and significant increase in use of piperacillin/tazobactam (15 v. 48, p<0.0001) after protocol implementation. 26 (17.3%) patients received probiotics ordered in the pre-protocol group while 55 (36.7%) patients received probiotics after protocol implementation (p<0.001). Of the 55 patients in the post-protocol who received probiotics, 36 (65%) orders were initiated by pharmacists per the probiotic protocol. 10 of 11 patients with CDI did not have a documented penicillin allergy. Of these patients, 3 received levofloxacin, 3 received piperacillin/tazobactam, 2 received meropenem, 1 received cefepime and 1 received ceftriaxone.

Conclusions: The implementation of a pharmacist-driven probiotic protocol significantly increased in the number of probiotics ordered, however pharmacist adherence was low and there was no significant difference in the number of CDI cases. Increased pharmacist adherence to the protocol is needed to provide a better comparison of probiotic efficacy in primary prevention of CDI.

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