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Editorial

Necessary Revision to Recommend Proton Pump Inhibitors to Hospital in patients Infected with *Clostridium Difficile*

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Clostridium difficile (*C. difficile*) as a gram-positive bacillus is the main cause of diarrhea leading to hospital admission. The term "*difficult clostridium*" is properly referred to the difficult approach in successful bacterial culture. Unfortunately, there is a great problem in hospitals in the case of unrecognized outbreaks caused by *C. difficile* (1-5). Several reports have shown a rapid increase in both the incidence and prevalence of *C. difficile* infection in many developing and developed countries (4,6,7). Thus, a concern of better policy toward this mysterious bacillus is logical and should be considered. Many guidelines have been released to improve the management of gastroduodenal disorders including *C. difficile*-linked disorders (8,9). In other words, relatively high mortality and morbidity rates have made this microorganism the focus of many studies (10). Infection with this problematic bacillus seems exacerbating the severity of digestive disorders such as colitis and self-limited diarrhea (11-13). Meanwhile, the increased epidemiology of *C. difficile* infection (CDI) in the current century is an alarming situation for all related diseases worldwide. In other hands, there is a general agreement that many factors affect the conditions of gastrointestinal biota including microbial colonization (14). As some primary studies showed significant improvement in the treatment of specific diseases using proton pump inhibitors (PPIs), we have increased recommendations to prescribe them as empiric therapy. Due to the intrinsic characters of PPIs, they have major effects on human microbiota (15), a complex interaction that never discussed. By now, there is no clear conclusion on the related consequences, but it has been predicted that uncontrolled prescription of PPIs can change the human microbiota ending in some severe digestive disorders. For example, wide-spread use of PPIs can inactivate H^+/K^+-ATPases resulting in achlorydria (16). Unfortunately, the misuse of PPIs in treating many gastroduodenal-related diseases can worry decision-makers to rethink or even restrict future recommendations of these universal drugs. Our main concerns about increasing use of PPIs are about recent increased outbreaks of CDI, both in hospitals and community (17). Epidemiological evidence shows that PPI-consumption is high in those patients colonized with *C. difficile* (18,19). Moreover, as there is a body of evidence on reasonable link between CDI and PPI consumption, this risk factor should be under intense attention by gastroenterologists and microbiologists. At least for patients who are admitted to hospitals for more than 7 days and may undergo a surgery or invasive test, computed tomography (CT) imaging is highly recommended because it is i) a non-invasive screening test and ii) it gives the opportunity to start appropriate antibiotic therapy. In conclusion, careful evaluation of the patients receiving PPIs admitted to hospitals who complain about signs like diarrhea regardless of their hospitalization can be a novel suggestion in current century. Fecal microbiota transplantation (FMT) can be a likely alternative treatment in improving the treatment level for those patients. However, this topic has not been discussed in guidelines and there is definitely a need to be elaborated in near future. Current knowledge about the impact of PPIs on human microbiota is deficient and needs further experiments in both animal and human models. The only necessary indication of PPIs

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use can be in patients with high risk of contamination with *C. difficile*. Meanwhile, several risk factors include dysbiosis and overgrowth by CDI should be considered in treatment of patients with gastroduodenal disorders. It seems necessary that the use of PPIs in patients colonized with *C. difficile* as a novel strategy should be propagated in clinical settings.

Keywords: Proton pump inhibitors (PPI), Clostridium difficile, Hospital inpatients, Antibiotics

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CONFLICT OF INTEREST

The author declares no conflict of interests related to this work.

REFERENCES

1. van Beurden YH, Dekkers OM, Bomers MK, Kaiser AM, van Houdt R, Knetsch CW, et al. An Outbreak of *Clostridium difficile* Ribotype 027 Associated with Length of Stay in the Intensive Care Unit and Use of Selective Decontamination of the Digestive Tract: A Case Control Study. *PloS One* 2016;11:e0160778.
2. Tamez-Torres KM, Torres-Gonzalez P, Leal-Vega F, Garcia-Alderete A, Lopez Garcia NI, Mendoza-Aguilar R, et al. Impact of *Clostridium difficile* infection caused by the NAP1/RT027 strain on severity and recurrence during an outbreak and transition to endemicity in a Mexican tertiary care center. *Int J Infect Dis* 2017;65:44-9.
3. Crobach MJT, Voor In 't Holt AF, Knetsch CW, van Dorp SM, Bras W, Harmanus C, et al. An outbreak of *Clostridium difficile* infections due to new PCR ribotype 826: epidemiologic and microbiologic analyses. *Clin Microbiol Infect* 2018;24:309.e1-309.e4.
4. Cassir N, Delaroziere JC, Dubourg G, Delord M, Lagier JC, Brouqui P, et al. A Regional Outbreak of *Clostridium difficile* PCR-Ribotype 027 Infections in Southeastern France from a Single Long-Term Care Facility. *Infect Control Hosp Epidemiol* 2016;37:1337-41.
5. Bouza E, Alcala L, Marin M, Valerio M, Reigadas E, Munoz P, et al. An outbreak of *Clostridium difficile* PCR ribotype 027 in Spain: risk factors for recurrence and a novel treatment strategy. *Eur J Clin Microbiol Infect Dis* 2017;36:1777-86.
6. Denève C, Janoir C, Poilane I, Fantinato C, Collignon A. New trends in *Clostridium difficile* virulence and pathogenesis. *Int J Antimicrob Agents* 2009;33:S24-8.
7. Quesada-Gomez C, Lopez-Urena D, Acuna-Amador L, Villalobos-Zuniga M, Du T, Freire R, et al. Emergence of an outbreak-associated *Clostridium difficile* variant with increased virulence. *J Clin Microbiol* 2015;53:1216-26.
8. Fekety R. Guidelines for the diagnosis and management of *Clostridium difficile*-associated diarrhea and colitis. American College of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol* 1997;92:739-50.
9. Kelly CP, LaMont JT. *Clostridium difficile*—more difficult than ever. *N Engl J Med* 2008;359:1932-40.
10. McDonald EG, Milligan J, Frenette C, Lee TC. Continuous proton pump inhibitor therapy and the associated risk of recurrent *clostridium difficile* infection. *JAMA Intern Med* 2015;175:784-91.
11. Surawicz CM, Brandt LJ, Binion DG, Ananthakrishnan AN, Curry SR, Gilligan PH, et al. Guidelines for diagnosis, treatment, and prevention of *Clostridium difficile* infections. *Am J Gastroenterol* 2013;108:478-98.
12. Kelly CR, Ihunnah C, Fischer M, Khoruts A, Surawicz C, Afzali A, et al. Fecal microbiota transplant for treatment of *Clostridium difficile* infection in immunocompromised patients. *Am J Gastroenterol* 2014;109:1065-71.
13. Youngster I, Russell GH, Pindar C, Ziv-Baran T, Sauk J, Hohmann EL. Oral, capsulized, frozen fecal microbiota transplantation for relapsing *Clostridium difficile* infection. *JAMA* 2014;312:1772-8.
14. Bakken JS, Borody T, Brandt LJ, Brill JV, Demarco DC, Franzos MA, et al. Treating *Clostridium difficile* infection with fecal microbiota transplantation. *Clin Gastroenterol Hepatol* 2011;9:1044-9.
15. Jackson MA, Goodrich JK, Maxan ME, Freedberg DE, Abrams JA, Poole AC, et al. Proton pump inhibitors alter the composition of the gut microbiota. *Gut* 2016:65:749-56.
16. Williams C, McColl K. Review article: Proton pump inhibitors and bacterial overgrowth. *Aliment Pharmacol Ther* 2006;23:3-10.
17. van Beurden YH, Hensgens MP, Dekkers OM, Le Cessie S, Mulder CJ, Vandenbroucke-Grauls CM. External Validation of Three Prediction Tools for Patients at Risk of a Complicated Course of *Clostridium difficile* Infection: Disappointing in an Outbreak Setting. *Infect Control Hosp Epidemiol* 2017;38:897-905.
18. Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of *Clostridium difficile* infection with acid suppressing drugs and antibiotics: meta-analysis. *Am J Gastroenterol* 2012;107:1011-9.
19. Dalton BR, Lye-Maccannell T, Henderson EA, Maccannell DR, Louie TJ. Proton pump inhibitors increase significantly the risk of *Clostridium difficile* infection in a low-endemicity, non-outbreak hospital setting. *Aliment Pharmacol Ther* 2009;29:626-34.