International Journal of Colorectal Disease (2019) 34:1503–1504
https://doi.org/10.1007/s00384-019-03335-w

LETTER TO THE EDITOR

Comments on "Supplementation with *Lactobacillus reuteri* ATCC PTA 4659 in patients affected by acute uncomplicated diverticulitis: a randomized double-blind placebo controlled trial"

Jiezhong Chen[1] · Luis Vitetta[1,2]

Accepted: 19 June 2019 / Published online: 26 June 2019

Dear Editor:

The intestinal microbiota has been associated with numerous disease states including diverticulitis, and probiotics have been used as an adjunct therapy for diverticulitis. We read with interest the article entitled "Supplementation with *Lactobacillus reuteri* ATCC PTA 4659 in patients affected by acute uncomplicated diverticulitis: a randomized double-blind placebo controlled trial" by Petruzziello and colleagues [1]. The authors elegantly demonstrated that the probiotic *Lactobacillus reuteri* decreased pain in patients diagnosed with diverticulitis and decreased blood levels of C-reactive protein, a marker of systemic inflammation. The hospitalization time of the patients diagnosed with diverticulitis was shortened, indicating that the probiotic showed efficacy in treating diverticulitis. However, the mechanisms for the probiotic bacterium to reduce inflammation are less well explored in the study. We posit that probiotic bacteria may encourage the intestinal microbiome to increase local butyrate production that could critically enhance repair of intestinal lesions caused by diverticulitis that is secondary to severe local colonic inflammation.

A recent study revealed that *Lactobacillus plantarum* increased butyrate-producing bacteria *Anaerotruncus* and *Faecalibacterium* with correlated increased production of fecal butyrate and acetate [2]. Increased short-chain fatty acids were correlated with increased tight junction integrity with increased expression of tight junction proteins claudin-1, occludin, and zonulin-1. The inflammatory cytokines IL-6, IL-8, and TNF-alpha were also observed to be decreased. It has been demonstrated that butyrate but not acetate can inhibit inflammation through the activation of regulatory T-cells [3]. Mechanistically the effect is through the activation of butyrate receptor GPR109A or inhibition of histone deacetylases [3, 4]. The depletion of regulatory T-cells abrogated the anti-inflammatory effect of butyrate, indicating that these cells are of critical importance [4].

In recognizing the importance of butyrate as a modulator of the anti-inflammatory response in diverticulitis is of clinical significance. The further development of probiotics to further downregulate colonic pro-inflammatory responses could be improved by formulating synbiotics with the addition of prebiotic fibers. Probiotic bacteria such as *Lactobacilli* do not themselves produce butyrate directly but facilitate and encourage the increased production of butyrate by butyrate-producing bacteria in the intestinal microbiome. The efficacy is also dependent on available fibers for fermentation. Dysbiosis in diverticulitis may reduce optimal production of butyrate. The administration of probiotic bacteria that can influence the colonic bacterial cohort may further increase the production of butyrate and thus significantly attenuate pro-inflammatory activity in the colonic mucosa whilst aiding repair of the colonic epithelia.

✉ Jiezhong Chen
jiezhong_chen@medlab.co

✉ Luis Vitetta
luis.vitetta@sydney.edu.au; luis_vitetta@medlab.co

[1] Medlab Clinical Ltd., Sydney 2015, Australia

[2] The University of Sydney, Faculty of Medicine and Health, Sydney 2006, Australia

References

1. Petruzziello C, Migneco A, Cardone S, Covino M, Saviano A, Franceschi F, Ojetti V (2019) Supplementation with Lactobacillus reuteri ATCC PTA 4659 in patients affected by acute uncomplicated diverticulitis: a randomized double-blind placebo controlled trial. Int J Color Dis 34(6):1087–1094

2. Wang J, Ji H, Wang S, Liu H, Zhang W, Zhang D, Wang Y (2018) Probiotic Lactobacillus plantarum promotes intestinal barrier function by strengthening the epithelium and modulating gut microbiota. Front Microbiol 9:1953
3. Chen J, Vitetta L (2018) Inflammation-modulating effect of butyrate in the prevention of colon cancer by dietary fiber. Clin Colorectal Cancer 17(3):e541–e544
4. Furusawa Y, Obata Y, Fukuda S, Endo TA, Nakato G, Takahashi D, Nakanishi Y, Uetake C, Kato K, Kato T (2013) Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. Nature 504(7480):446–450