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POLYAMINES ACTIVITY IN CANINE INFLAMMATORY COLORECTAL POLYPS BEFORE AND AFTER A PROBIOTIC BACTERIA TREATMENT

Giacomo Rossi¹, Matteo Cerquetella¹, Silvia Scarpona¹, Sara Berardi¹, Andrea Piccinini¹,
Subeide Mari¹, Gian Enrico Magi¹, Graziano Pengo² and Jan S. Suchodolski³

¹School of Biosciences and Veterinary Medicine, University of Camerino

²Veterinary clinic "San Antonio", Cremona

³Gastrointestinal Laboratory, Texas A&M University, College Station, USA

Recent researches demonstrate a correlation between polyamine intake or intestinal exposure, to risk of colorectal neoplasia (Vargas et al., 2012). Furthermore, the role of polyamines, spermidine (SPD) and spermine (SPM), and their precursor putrescine (PUT), regulated in their cellular levels by ornithine decarboxylase (ODC), in cell growth and proliferation is very well recognized. Increased polyamine levels are observed also in patients with IBD with their corresponding inflammatory index revealed that increased concentrations of polyamines found in the most severe inflamed mucosal areas. Some probiotics seem to have anti-inflammatory and tumor inhibitory properties, but few studies have investigated their actions on mucosal polyamine levels. Recently, a demonstration that dysbiosis is associated with canine inflammatory colorectal polyps (ICRPs) development, and that this may represents a potential therapeutic target, was published (Igarashi et al, 2016). In this study, the effects of probiotic mixture on colonic polyamine biosynthesis in dogs with colonic polyposis (CP) were investigated. Histological sections of dogs with a long-time diagnosis of colonic polyposis (n=5) were analyzed. These dogs had received between 112 and 225 billion (112 to 225 x 10⁹) of lyophilized bacteria daily for 60 days, and samples were obtained at baseline (T0) and 30 days after the end of treatment (T1; i.e. 90 days after T0). Histology scores, the expression of PUT, SPM, ODC and DAO positive cells, and the clinical activity index (CIBDAI) were compared at T0 and T1 using paired t-tests or Wilcoxon matched pairs tests, where appropriate. Additionally, levels of cellular proliferation (Ki-67 expression), and apoptosis (Caspase 3 protein expression) in the polyp were also evaluated. After probiotic treatment, significant decreases were observed for CIBDAI (p=0.006) and histology scores (p<0.001). In

contrast, SPM, PUT, and ODC expression increased ($p < 0.01$) after probiotic treatment. Specifically, a significant decrease in colonic polyamine levels, ODC activity and Ki-67 was noted at T1 to T0. In contrast, a significant increase in caspase-3 positive cells and DAO expression ($p = 0.005$) was also observed. Polyamines levels suggest a potential anti-proliferative effect of probiotics in hyperplastic mucosa, but also an anti-inflammatory effect associated with a reduction of mucosal infiltration. These effects could be related to increase in some bacteria genera such *Faecalibacterium* after probiotic treatment. Interestingly *Faecalibacterium* catalyzes the irreversible transfer of a propylamine group from the amino donor S-adenosylmethioninamine (decarboxy-AdoMet) to putrescine (1,4-diaminobutane) to yield spermidine, increasing PUT and SPD levels (van Vliet MJ, 2010). In conclusion, this study provides data about the ability of a cocktail of probiotics, administered for 8 weeks, to regulate polyamine levels, by enhancing polyamine biosynthesis and degradation in canine inflamed polypoid colonic mucosa, and to reduce cell proliferation in hyperplastic/neoplastic areas.



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SAFOOD srl
L.go Braccini 2
10095, Grugliasco (TO)
direzione@safood.it