COMMENTARY

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Should dental care professionals prescribe probiotics for their patients under antibiotic administration?

More than 20 million antibiotic prescriptions are written by general dentists in the outpatient setting.[1] Antibiotic agents, such as penicillins, lincosamides and macrolides, are widely prescribed by dentists.[1] Qualitative evidence suggests that inappropriate prescribing of antibiotics is a common practice in dentistry.[1] The unnecessary use of antibiotics promotes global health problems, such as dysbiosis and bacterial resistance to antibiotics.[2] Ingestion of antibiotic produces gut dysbiosis (namely alteration of the function and diversity of bacteria in the intestinal microbiome) in patients.[3,4] In addition, dysbiosis of the gut microbiome can be induced by other factors, such as type of diet and lifestyle habits.[2] Approximately 30–400 trillion microorganisms inhabit the healthy intestinal tract in humans.[4] The main contributions of these symbiotic bacteria to the human host are the prevention of pathogen colonisation, immunomodulatory activity, lymphoid tissue development, vitamin synthesis and carbohydrate metabolism.[4] Moreover, the gut microbiome induces the dendritic and follicular dendritic cells to produce immunoglobulin A-secreting plasma cells, and in turn, immunoglobulin A regulates the composition and function of the intestinal microflora.[4] Consequently, an imbalance of the gut microbiome can result in dysbiosis-related diseases in patients, such as increased susceptibility to infectious diseases, altered immune homeostasis, allergic diseases, metabolic syndrome, obesity and others.[2,4] Alterations in the gut microbiome caused by exposure to systemic antibiotics are usually reversed within 2 months.[2] However, the modified microbial profile may continue for longer periods of time in some patients.[2] This latter situation increases the risk of developing dysbiosis-related diseases.[2] Therefore, protecting the gut microbiome during antibiotic therapy should be a priority for the dental care professional.

Diarrhoea, gastric pain and nausea are linked to dysbiosis.[2] Antibiotic-associated diarrhoea (AAD) may occur during antibiotic treatment but also after the antibiotic has been discontinued.[5] A high risk for the development of AAD is caused by the administration of aminopenicillins with/without clavulanic acid, cephalosporins, clindamycin, fluoroquinolones or antibiotics with activity against anaerobes.[3,5] Consequently, AAD is a visible sign of dysbiosis associated with antibiotics when other causes of diarrhoea are absent. The clinical presentation of AAD may vary from mild diarrhoea to fulminant pseudomembranous colitis,[6] and the prevalence of AAD ranges from 5% to 80% in children and adults.[3,5,6] The prevalence of AAD increases with duration of antibiotic intake and when different antibiotics are combined. The use of probiotic bacteria such as *Saccharomyces boulardii* or *Lactobacillus rhamnosus* GG for preventing AAD is recommended by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Working Group on Probiotics and Prebiotics as well as by recent systematic reviews.[5,7–9] The use of *L. rhamnosus* GG or *S. boulardii* reduces the risk of AAD in approximately 50% of patients.[3,9] AAD is prevented by these probiotics through several mechanisms.[3,6] *Lactobacillus rhamnosus* GG and *S. boulardii* compete with bacterial pathogens for attachment sites on intestinal cells. Subsequently, these probiotics may exert their biological activities,[3,6] such as modulating the content of gut microbiota, maintaining the integrity of the intestinal barrier, preventing bacterial translocation and modulating the immune response.[7]

When administered in appropriate quantities, probiotic bacteria provide benefits to the host.[4] A daily dose of 250–500 mg (children) or 200–1,000 mg (adults) of *S. boulardii* can be used to reduce the risk of AAD.[6] This probiotic can be administered either for the duration of antibiotic treatment (adults and children) or started within 48 hours of antibiotic therapy and maintained until the course of antibiotic is complete (adults only). Also, in adults, probiotic therapy may be continued for 2 weeks after antibiotic therapy is complete.[6] The dosages of probiotic mentioned earlier in this paragraph were obtained from a meta-analysis of 21 clinical trials.[6] That meta-analysis showed a significant, beneficial effect in favour of *S. boulardii* (risk ratio = 0.47; 95% CI: 0.38–0.57; $P < 0.00001$).[6] This yeast can be administered simultaneously with antibiotics because it is not affected by

these agents.[10] Under probiotic therapy with this yeast, antibiotics were administered to patients during a period of 5–14 days.[6] Meanwhile, a daily dose of 1–80 × 10^9 or 6–120 × 10^9 colony-forming units of *L. rhamnosus* GG may prevent AAD in children or adults, respectively.[3] For this probiotic, the dosages were obtained from a meta-analysis of 11 clinical trials.[3] That meta-analysis showed a significant, beneficial effect in favour of *L. rhamnosus* GG (risk ratio = 0.49; 95% CI: 0.29–0.83; $P = 0.008$).[3] Those studies reported that the probiotic was administered during and for 1 week after antibiotic therapy in adults but only during the period of antibiotic therapy in children.[3] To obtain a beneficial effect, this probiotic should be taken at least 1.5 hours after administration of antibiotic.[10,11] The co-administration of *L. rhamnosus* GG with an antibiotic agent has a detrimental effect on the clinical efficacy of this probiotics because this bacterial strain is sensitive to antibiotics.[10] In this case, the antibiotics were administered to the patients for a period of 7–14 days.[3]

The use of probiotics should consider patient risk factors, such as the class of antibiotic, duration of antimicrobial treatment, age, comorbidities and presence of previous episodes of AAD.[5] Therapies using *S. boulardii* or *L. rhamnosus* GG are both safe and well tolerated by patients, including those of extreme ages.[3,6,7] Available evidence did not show that patients using probiotic organisms experienced a significantly larger number of adverse events (gastrointestinal events, infections, infestations or others) in comparison with a control group of participants.[5] However, probiotics should be used with caution in specific patient groups. Immunosuppression, prematurity, critical diseases, presence of structural heart disease, presence of a central venous catheter and possible translocation of probiotics across the gut barrier are risk factors for the development of adverse reactions as a result of probiotic use.[5] For example, *S. boulardii* caused fungaemia in patients with life-threatening conditions who were managed in intensive care units.[6] Dental care professionals should be aware of possible variations in the effectiveness and safety profile of commercial products. The influence of the manufacturing process on the properties of probiotic bacteria remains unclear.[5] Ultralevure® (Biocodex, Montrouge, France), Enterol® (Biocodex), Giflorex® (Errekapa Euroterapici S.p.A., Milan, Italy) and capsules obtained from CAG Functional Foods (Omaha, Nebraska) are some commercial products that have demonstrated clinical efficacy in previous studies.[3,6] Probiotics with potential for use in treatment of AAD, but for which there is currently insufficient scientific evidence to make a recommendation, are *Bacillus clausii*, several mixtures of probiotics, kefir and yogurt.[5] Examples of strain mixtures are *Bacillus lacticus* plus *Streptococcus thermophilus*, *Lactobacillus acidophilus* plus *Lactobacillus bulgaricus*, and *L. acidophilus* plus *Bifidobacterium infantis*, among many others.[5] Many different strains, products and combinations of probiotics are commercially available. However, health-care professionals and consumers have to make decisions about the use of probiotics considering the actual scientific evidence available and professional advice. To our knowledge, there is no information available on the use of probiotics when antibiotics are prescribed for dental procedures and infections. Moreover, current guidelines do not consider prescribing probiotics for dental patients.[12–15]

In conclusion, dental-care professionals prescribing antibacterial medication should consider the gut dysbiosis associated with these drugs and take the opportunity to treat their patients appropriately. The use of probiotics reduces the risk of development of gut dysbiosis associated with ingestion of antibiotic alongside many dysbiosis-related systemic diseases. *Saccharomyces boulardii* and *L. rhamnosus* GG are the probiotics for which there is sufficient scientific evidence to support their use. Probiotic therapy should be started as soon as possible after ingestion of antibiotic. It is important to note that different dosages of these probiotics have been established for children and adults. As a result of the antimicrobial susceptibility of the lactobacillus, a period of ≥1.5 hours is required for all patients between ingestion of the antibiotic and ingestion of the probiotic.

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Conflict of Interest

The authors declare no conflict of interest, including any financial, personal or other relationships with people or organisations.

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