CHRONIC RHINOSINUSITIS AND PROBIOTICS: A REVIEW

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ABSTRACT

Background: Probiotics are already used for the treatment of certain functional disorders. Despite a well-conducted medico-surgical treatment, the proportion of chronic sinusitis remains important.
Objective: To determine the contribution of probiotics in the management of chronic rhinosinusitis from a review of the literature.
Data source: We carried out a two-step bibliographic search, covering English-language publications from 2014 to 2015, using the Pubmed engine. In the first step, the key words were "probiotics" and "chronic rhinosinusitis". For the second step, the key words were "sinus microbiome", "probiotic's mechanism action" or "probiotic's study". We retained 17 publications out of 119.
Data synthesis: There is no consensus on the sinus microbiome. The *lactobacillus* strains were the most tested. Probiotics used for prevention or adjuvant treatment mainly through the nasal route appear to be more effective.
Conclusion: The efficacy of nasal probiotics has been demonstrated in adjuvant therapy and prevention.

Key words: Probiotics, Rhinosinusitis, Chronic

INTRODUCTION

Probiotics are living microorganisms which, when given in adequate quantities, produce a health benefit for the host[1]. They would help to eliminate the responsible germs and stimulate the useful germs. Probiotics that would help restore the bacterial ecosystem are already used for the treatment of certain functional disorders in gastroenterology, gynaecology and dermatology[2,3]. In ENT, we could compare the cases of imbalance of the bacterial ecosystem (dysbiosis) favoring chronic rhinosinustitis. Indeed, the passage to chronicity of rhinosinusitis despite a well-conducted medico-surgical treatment would be due to a significant inflammatory phenotype. This phenotype, expression of persistent inflammation, affects approximately 30% of patients[4,5]. Would probiotics, supposed to restore the bacterial ecosystem, be useful in the treatment of chronic rhinosinusitis? Based on a review of the literature, this work aims to respond to these concerns.

DATA SOURCE

We carried out a two-step bibliographic search, covering English-language publications from the year 2014 to 2015, using the Pubmed engine. The first step consisted of searching for publications using the keywords "probiotics" and "chronic rhinosinusitis". We obtained 14 publications of which nine were selected because they answered the appropriate combination "probiotics and chronic rhinosinusitis". The bibliographic search covered both clinical and laboratory studies, in humans as well as in animals. In the second stage, the bibliographic search consisted of consulting on Pubmed the 110 bibliographic references of previously selected publications. A reference was chosen when the terms "sinus microbiome", "probiotic's mechanism action" or "probiotic's study" were found. We therefore retained eight other publications, for a total number of 17 publications out of 119.

DATA SYNTHESIS

Sinus microbiome

There is no consensus on the exact make up of the sinus microbiome. It is polymicrobial and essentially composed of *pseudomonas, staphylococcus*, and *streptococcus*[6]. Other bacteria such as f*irmicutes* (*Lactobacillus, actinobacteria) propionibacterium*, and b*acteroidetes* have been reported[7,8]. These saprophytic bacteria can under certain conditions become pathogenic. The diversity of the microbiome prevents the proliferation of a group of bacteria that later become pathogenic. The microbiome stimulates baseline immunity by interacting with the epithelium maintaining baseline inflammatory activity[9].

Mechanism of action of probiotics

Probiotics modulate the immune system through an anti-inflammatory effect and inhibit pro-inflammatory

cells[10]. Gram-positive probiotics *lactobacilluslactis* have an anti-inflammatory effect through Interleukin 10 and inhibit pro-inflammatory cells globally (nuclear factor)[10]. On the other hand, *staphylococcus aerius* has a dependent bacterial load effect. In small amounts, it has a strong anti-inflammatory effect and inhibits pro-inflammatory cells. It behaves like a saprophytic germ which stimulates immunity. In large quantities, it has the opposite effect[10]. Probiotics produce antimicrobial agents. They promote pH variation. Probiotics compete to avoid colonization of the sinus by a pathogenic species and for receptor binding. *Lactobacillus reuteris* are produced by the protein euterin. It induces oxidative stress in competing proteins[11]. *Lactobacillus spp.* produces acetic and lactic acid thus reducing the pH, thus inhibiting the growth of acid-intolerant taxa[12-14]. *Lactobacillus johnsonii* competes at the receptor level (asialo-GM1) with *pseudomonas aeruginosa*, *haemophilus influenzae* and *Staphylococcus aureus*[15].

Clinical tests

Habermann *et al*[16] reported a multicenter double-blind study involving 157 patients. It was based on oral administration of *enterococcus faecalis* in 20 drops to 30 drops three times a day for six months. This study observed a significant reduction in sinusitis attacks with a decline of eight months after treatment. The probiotic *enterococcus faecalis* has been used as an adjuvant in 204 children with recurrent sinusitis[17]. The children were treated with amoxicillin and a nasal decongestant for seven days. Then *enterococcus faecalia* was administered at the rate of 20 drops three times a day orally for eight months. This study demonstrated a regression in the frequency and duration of attacks.

A randomized clinical test involving 77 patients by Mukerji *et al*[18] evaluated the efficacy of oral administration of probiotics in patients with chronic rhinosinusitis. *Lactobacillus rhamnosus* was administered in tablet form (containing 500 million active strains) twice a day for four weeks. The condition of the patients did not improve compared to the control group. Martensson *et al*[19] performed a randomized, double-blind study of 21 patients with chronic non-polyp rhinosinusitis. They studied the effect of nasal (spray) administration of *lactobacillus* from bees for two weeks. They concluded that there was good tolerance without any impact on the severity of the symptoms, nor of the microbial flora as well as of the local anti-inflammatory activity[19]. Roberta *et al*[20] carried out a study on 20 healthy people on the administration by the nasal route (spray) of a mixture of *streptococcus salivarius* 24SMBc and *streptococcus oralis* 89 for one week each morning after visiting the toilet. They observed a week after the end of the treatment a significant increase in 2 germs and a significant regression of *staphylococcus aureus* in the nasal secretions of healthy people. The comparison of the bacterial species in the nasal mucosa of healthy people before and after one month of treatment showed the reduction of the bacterial species in relation with a proliferation of pathogenic bacterial germs[20]. Uehara *et al*[21] found a low incidence of colonization of *staphylococcus aureus* in the nasal vestibules of 156 patients carrying c*orynebacterium tuberculostearicum*. Nasal administration of *corynebacterium tuberculostearicum* in patients with *staphylococcus aureus* resulted in the eradication of *staphylococcus aureus* in 71% of cases[21]. Abreu *et al*[7] studied the microbiome of patients suffering from chronic rhinosinusitis to identify the most common pathogenic bacteria. In a second step, they tested the efficacy of a bacteria against them using mice as a human mode of rhinosinus infection. They first studied the microbiome of patients (n=10) with chronic rhinosinusitis and healthy people (n = 10). They noted a predominance of c*orynebacterium tuberculostearicum* in patients with chronic rhinosinusitis. The abundance of c*orynebacterium tuberculostearicum* correlated with the severity of chronic rhinosinusitis. Second, the mouse (n = 20) was used as a model for rhinosinus infection to test the efficacy of *lactobacillus sakei* against c*orynebacterium tuberculostearicum*. The simultaneous administration in mice (previously treated with antibiotic therapy) of *Lactobacillus sakei* and c*orynebacterium tuberculostearicum* by the intranasal route compared to the single administration of *corynebacterium tuberculostearicum* made it possible to demonstrate a significant reduction in *corynebacterium tuberculostearicum* in the group having received the probiotic and the pathogen[7]. This would suggest a competitive inhibition of the proliferation of *corynebacterium tuberculostearicum* by l*actobacillus sakei*.

Cleland *et al*[22] studied the administration of *staphylococcus aureus* and *staphylococcus epidermis* intranasally in 20 mice divided into two groups[22]. *Staphylococcus aureus* and *staphylococcus epidermis* were administered in one group and single administration of *staphylococcus aureus* in the other group. They found a significant reduction in *staphylococcus aureus* in the group of mice receiving

the two germs. This suggests the probiotic potential of *staphylococcus epidermis* vis-à-vis *staphylococcus aureus* which is a recalcitrant germ in chronic sinusitis[22].

CONCLUSIONS

The exact composition of the sinus microbiome is not known. But the imbalance of bacterial species in the sinuses is a characteristic feature of chronic bacterial rhinosinusitis. Probiotics oppose pathogenic bacteria by two mechanisms. The first is competition for sinus space and receptors. The second is the secretion of antimicrobial substance. Lactobacillus strains have been the most widely used probiotics. Their administration by the nasal route was the most favoured. Probiotics used for prevention or as an adjuvant have proved more effective than using them alone to treat chronic bacterial rhinosinusitis.

The efficacy of probiotics has been demonstrated in the adjuvant therapy and prevention of chronic bacterial rhinosinusitis. *Lactobacillus* strains have been the most tested probiotics; the nasal route is thought to be the most favoured.

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