Perspectives of Probiotic Therapy in Sinus Infection

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Introduction: Sinusitis are the nation’s primary chronic health problem in USA and many other countries. Sinusitis is a term which refers to inflammation of the lining of the sinuses, called mucosa. Things that can trigger inflammation of the mucosa are a cold, allergies, a deviated septum, reflux disease, nasal polyps and certain chronic diseases. This inflammation can block the narrow passages in the sinuses and prevent mucus from draining properly leading to infection. As a bacterial reservoir, the nose may harbor potentially pathogenic bacteria (PPB) Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Moraxella catarralis, β-hemolytic streptococci and others, including fungal pathogens. In patients carrying PPB, effective antibiotic regimens without negative side effects could be crucial for infection control after major operations on or injuries of the head, nasal sinuses, or lungs. Such regimens may also be important for diabetic patients and persons receiving hemodialysis, in intensive care units, or with impaired immunity due to various other causes.

The causes of sinusitis are numerous and varied. Some of these causes could be treated through avoidance and medications, although for some, surgical treatment may be necessary. The most commonly used surgical treatments, in the case of an acute, chronic, or recurrent sinus infection, include antibiotics, steroids, antihistamines, mucus thinning agents, decongestants, pain relievers and saline irrigation sprays. Most of these medications may lead to unwanted long-term side effects. Antibiotics, in particular, can have digestive side effects, which lead to excessive diarrhea. Currently, Probiotics are used to treat sinusitis by increasing the amount of healthy bacteria in the gut, thereby reducing the amount of diarrhea and other digestive complications. Our aim is to create Target-Specific Probiotics that address the root causes of sinus infections and improve the stability of health benefits for sinus structures and tissues, high levels of antibacterial activity against specific pathogens, anti-allergy and anti-inflammation activity, the ability to regulate local immune reactions, and have no negative side-effects and improve the patient's health.

Methods: Previously selected and characterized by FAA/WHO recommendations, strains of Lactobacillus delbrueckii LE and Lactobacillus rhamnosus LB3 as well as in combination (LE+LB3 blend) in the concentration of 5 x 10^8 cells/dose, were used in the study. (Figure 1) in vitro tests were performed to check the ability of probiotic candidates to inhibit growth of specific bacterial and fungal pathogens and to assess adhesion properties to nasal epithelial and adenoid cells. In vivo trials were conducted on marine models and on humans to evaluate the ability of individual strains and their combinations to demonstrate immune activity, including cytokine and antibody production and regulation, competitive exclusion of pathogens, such as bacteria and fungi, and its efficacy to treat chronic sinus diseases. The immune regulation potency of the probiotic formulations were tested under conditions of immunodeficiency. The immunodeficiency model in mice was designed using a cyclophosphamidic maneuver in the dose of 50 mg/kg a day before the intake of the probiotics.

Additionally, for the purpose of testing the immune potency of the probiotic formulations, the tonsillar cells from the patients with adenoid disease were cultivated with the medications for 4 hours, at which point the number of Immunoglobulin Fc fragment receptor cells and the antigen CD25 and CD56 natural cytotoxic cells of IgA-producers were tested. In clinical conditions, the preparations were prescribed in one dose (2 x 10^6 - 5 x 10^7) once a day during a ten-day trial. For ablation of the lacunae of the faunal tonsils in patients with chronic tonsilitis and gynemytrums in the patients with maxilloethmoidal sinusitis, the medications were dissolved in 20 ml of normal saline solution. As ablation control, in existent treatment with antibiotics and antifungal substances were used. Along with the existing treatments, as comparative agents, the probiotic drug, Linex (LEK, Slovenia) and therapeutic yohurt (Institute Rosel, Canada) were also used.

Researches. Researches indicated high levels of antagonistic activity towards the most frequent microbes found during recrudescence of invasive lemic-inflammatary diseases of ENT organs. (Figure 2) showed high degree of conjugation to mucous coat of the upper air passages, (Figure 3) and demonstrated acid and alkaline tolerance. Furthermore, L. rhamnosus LB3 was able to suppress growth of 90% of Candida strains, including Calbicans,C.krusei, C.tropicalis, (Figure 4)

It was reported that application of the formulation based on L. rhamnosus LB3 resulted in the statistically reliable increase of the number of tonsillar cells producing IgA as well as L. delbrueckii LE increased activity of the natural cytotoxic tonsillar cells against xenobiotics. (Figure 5)

It was observed that probiotic formulations stimulated IFN up to 4.5-fold, induced production of the IL-4, increased IgG and IgA up to 2.5 fold, and intensified glycoprotein synthesis in phagocytes. L. rhamnosus LB3 demonstrated more effective activation of humoral immune response; whereas, L.delbrueckii LE showed mostly cell-mediated immune response. (Figures 7 & 8)

In clinical conditions, combination of LB3 and LE demonstrated positive results in 85.5% cases of the chronic tonsilitis and 90% in maxilloethmoidal sinusitis as compared to positive results in 72.8% cases in the control patient group using antibiotics and antifungal substances. Performance capability was increased in 100% cases, the physiologic flora was restored, the amount of the pathogenic and opportunistic flora was reduced in 4-6 times, enzymatic activity was restored to the normal level and immune parameters were normalized. Probiotics were well-tolerated by the patients, demonstrated high clinical result and have had a positive effect on the microflora of the upper air passages. The comparative agents of Linex and yogurt were not statistically effective.

Conclusions. The new probiotic strains of L.delbrueckii LE and L. rhamnosus LB3 were deeply investigated and demonstrated their marked capacities for use in the development of target specific probiotic products for ENT infection and inflammation diseases. (Figure 9) The results also indicated that specific probiotic products and probiotic therapy treatments as reduce PPB in the upper respiratory tract as well as eliminate or reduce possible post treatment negative side effects and/or complications. Therefore, probiotic formulations based on LB3 and LE strains proved to be more efficient and active compared to the existing treatment and the comparative agents.