

PROTOCOL: Probiotics for Chalaziosis Treatment in Children

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Approved by CTS of Department of Medicine and Health Sciences “V. Tiberio” of Molise University on the 07 th January, 2019

The trial was registered at clinical trials.gov as NCT04322500 on the 25 th March, 2020 (“retrospectively registered”)

PURPOSE: Human gut holds over 100–1000 microbial species, which primarily modulate the host internal environment and thereby, play a major role in host health. Supplementation with probiotics has shown promising results against various enteric pathogens thanks to their unique ability to compete with pathogenic microbiota for adhesion sites, to alienate pathogens or to stimulate, modulate and regulate the host's immune response by initiating the activation of specific genes in and outside the host intestinal tract. [R. G. Kerry et al, *Benefaction of probiotics for human health: A review*, 2018] In recent years, intestinal microbiota emerged as a candidate responsible for providing innate stimuli to prime the immune system, and its contribution to pathogenesis of autoimmune diseases has been intensively studied. Clinical studies support a link between changes in gut commensal microbiota (‘dysbiosis’) and human autoimmune diseases including rheumatoid arthritis, spondyloarthritis, lupus, diabetes, inflammatory bowel disease and multiple sclerosis [McLean MH, Dieguez D Jr, Miller LM, et al. *Does the microbiota play a role in the pathogenesis of autoimmune diseases? Gut* 2015; Scher JU, Littman DR, Abramson SB. *Microbiome in inflammatory arthritis and human rheumatic diseases. Arthritis Rheumat* 2016; Ochoa-Reparaz J, Kasper LH. *The influence of gut-derived CD39 regulatory T cells in CNS demyelinating disease. Transl Res* 2017]. Moreover, animal studies on autoimmune uveitis in rodents have unraveled strong associations of gut microbiota with disease. Also ocular conditions such as chalazia are linked to dysbiosis [*Infective and Inflammatory Eyelid Disorders: Conventional and Unconventional Therapies to Maintain Eye Health and Avoid Lid Surgery*; A. L. Giacomini, *EC Ophthalmology* 2016]. Moreover, it is well known that any eating disorders such as excessive use of saturated fats, can result in a change in the composition of the secreted fat of the Meibomian glands, making it less fluid. So it becomes difficult to spill the glandular secretion leading to chalazia formation. The

correlation between inflammatory conditions of the conjunctival membrane, lacrimal dysfunctions and an intestinal immune condition featuring dysbiosis are pathophysiological conditions of great interest and are currently analysed. To the best of our knowledge there are no studies on probiotics supplementation in chalaziosis. Moreover, several evidence demonstrate that probiotics may play a role in the prevention and treatment of different conditions not only in adults, but also in children. In the latter population acute diarrhea is an important application of probiotics (Lactobacillus rhamnosus and Saccharomyces boulardii reduce the duration of gastroenteritis by approximately 24 h) [*The good bugs: the use of probiotics in pediatrics. Sansotta N, Curr Opin Pediatr.2019*]. Hence, this study aims to define the possible beneficial impact of probiotics on children suffering from chalaziosis.

DESIGN: This is a simple blind observational study. Paediatric patients affected by chalaziosis will be recruited. These patients will be divided in two groups, one receiving a supplementation with probiotics and the other one not. Prior to enrollment in the study all patients will undergo a complete ophthalmological examination which includes : visual acuity test, slit lamp for annexes and anterior segment assessment, ocular fundus examination, intra ocular pressure measurement. Subsequently a complete ophthalmological evaluation will be done weekly during the first month and then monthly until the healing. The ophthalmologist will be masked.

ATTENDED RESULTS: Altering the intestinal microbioma with specific probiotics can ameliorate the clinical course of chalaziosis by re-establishing intestinal and immune homeostasis. So, we expect to observe a reduction or absence of the recurrences of chalazia.

CONCLUSIONS: The use of probiotics for clinical health benefits is a fascinating area of research that the present era has yet to explore. Some of the elite properties of probiotics, such as anti-pathogenicity, anti-diabetic, anti-obesity, anti-inflammatory, anti-cancer, anti-allergic, and angiogenic activities and their effect on the brain and central nervous system are quite known. This study will provide further informations on probiotics and human health. Moreover, the intestinal microbiota are potentially crucial in spreading inflammatory disease of the eye, and can be targeted for therapeutic effects. So, throughout our study will be highlighted that probiotics supplementation could increase the effectiveness of traditional therapies in reducing recurrences of chalaziosis in an easy and feasible way.

Statistical Analysis Plan

Mann Whitney U test will be used in order to analyze if there will be a significant difference between the two groups in:

- Time taken for complete resolution of the chalazion
- Number of recurrences