THE NEW ADDRESSING PROBLEM IN INTESTINAL CANDIDOSIS

Suzana Otašević1,2, Milan Golubović1,4

1Department of Microbiology and Immunology, Faculty of Medicine, University of Niš, Niš, Serbia
2Institute of Public Health, Niš, Serbia
3Clinic of Paediatrics, Clinical Center Niš, Niš, Serbia
4Faculty of Medicine, University of Niš, Niš, Serbia

Abstract. Herein, we discussed a new problem concerning diagnosis, treatment, and monitoring of patients with intestinal candidosis. The lack of official attitude about the significance of Candida overgrowth on intestinal mucosa as well as the absence of guidelines regarding its treatment and required diet, significantly complicate this problem in medical practice. Possible overgrowth of species Saccharomyces cerevisiae-bulardi from probiotics in intestines is a newly recognized problem in diagnostic procedures.

Key words: intestinal candidosis, Candida overgrowth, Saccharomyces cerevisiae-bulardi.

Introduction

The role of Candida spp. in the etiology of gastrointestinal disturbances, infection, and diseases hasn’t been clarified yet. Gastrointestinal candidosis is still a subject of controversy in scientific circles without a unique opinion about pathogenic potential of this yeast, interpretation of mycological analysis result, and, most importantly, without referral guidelines for its treatment. Lack of official recommendations regarding this problem, alongside a huge number of unreliable theories and misbeliefs in referent literature, electronic media and newspapers, have confused both scientists and laymen since the 1980s [1-3].

Valid Postulates

We can point out following facts:

- It is well known that Candida spp. represent the part of gut microbiota (normal gastrointestinal flora) in healthy people, but in certain cases, these commensal fungi can convert from non-pathogenic to pathogenic ones [4].
- The most important Candida infections of the gastrointestinal tract are esophageal and gastrointestinal candidosis in severely immunocompromised. Esophageal candidosis is usually seen in AIDS patients or those receiving long-term chemotherapy. In addition, patients with leukemia and other hematologic malignancies are at increased risk for the development of multiple ulcers on the intestinal mucosa due to fungal infection. Thus, gastrointestinal perforation and complications such as peritonitis or hematogenous spread of fungi to the liver, spleen, and lungs are common in these patients [5].
- A big portion of healthy, immunocompetent, people having Candida spp. in their digestive system as part of microbiota, therefore have positive laboratory findings (positive Candida-isolates from the stool samples). For this reason, the discrimination between Candida-colonization and Candida-infection is difficult [6].
- Unlike obligate pathogens, whose detection implies disease, differential diagnosis between Candida-infection and Candida-colonization is more complex. In order to make a distinction, it is necessary to perform endoscopic biopsy and subsequent histopathological examination. This is the reason why there is still no unique approach regarding the treatment of patients with gastrointestinal candidosis and there are a lot of questionable viewpoints regarding the pathogenic effect of Candida on the intestinal mucosa.
- Regardless of many controversial postulates about pathogenic potential of Candida, current opinion in medical theory and praxis is that Candida spp. has a role in the occurrence of diarrhea after antibiotic consumption. Consequently, nystatin prophylaxis is recommended during the antibiotic treatment [7].
- The theory that immune dysregulation in intestinal mucosa, specifically IgE-mediated reaction to Candida antigens, actually leads to local and systemic damage of tissues is under investigation [8].
- There is still no official recommendation for antifungal “intestinal decontamination”. However the use of nystatin showed satisfactory anti-Candida effect with reduction and even complete withdrawal of symptoms in patients with diarrhea [7, 9].
Current Consideration and Observation

The presence of Candida yeast as a member of microbiota on intestinal mucosa is mainly benign. However, the results of the newest research concerning Candida spp. impact on the digestive tract, demonstrated that, if present, these yeasts may contribute to the destruction of already damaged mucosa. Studies that included patients with gastrointestinal diseases and the ones done on animal models, without a doubt revealed that presence of Candida may lead to an even bigger defect and massive inflammation [10-13].

Investigation of Crohn’s disease and the presence of Candida on intestinal mucosa established the relationship between this inflammatory bowel disease and intestinal Candida colonization [10]. Furthermore, it was demonstrated that antifungal treatment to reduce Candida-colonization lessens the severity of ulcerative colitis [11]. Moreover, analysis of the animal model suggested that Candida colonization may create a vicious cycle where yeasts slow down the healing of inflammatory lesions while inflammation promotes fungal colonization [12]. There is also an assumption that if Candida can cause infection and inflammation of the skin, severe damage of nail, inflammation of vulvovaginal mucosa, pseudomembranous and erythematous oral candidosis, a nail, inflammation of vulvo-vaginal mucosa, severe damage of gut flora, and dysbiosis of different flora. Based on this simplified, long-standing, concept and on our experience in routine work with patients who have Candida infection/colonization of digestive tract, we can point out that physicians usually prescribe local antifungal, with or without a diet, but recommendation of probiotics is practically mandatory. The role of microorganisms contained inside a probiotic supplement is to successfully colonize intestinal mucosa, stay resistant to the influence of other microorganisms, and persist in intestines. The use of these supplement products increases the possibility of gut colonization with non-pathogenic microbes and preservation of normal balance among usual members of physiologic flora [14].

Problems

In addition to these still unresolved issues, in practice, there are also problems of diagnosis and patients treatment. Candida spp. can, under the influence of various factors, multiply rapidly and overgrow the rest of gut microbiota, leading to dysbiosis. Based on this simplified, long-standing, concept and on our experience in routine work with patients who have Candida infection/colonization of digestive tract, we can point out that physicians usually prescribe local antifungal, with or without a diet, but recommendation of probiotics is practically mandatory. The role of microorganisms contained inside a probiotic supplement is to successfully colonize intestinal mucosa, stay resistant to the influence of other microorganisms, and persist in intestines. The use of these supplement products increases the possibility of gut colonization with non-pathogenic microbes and preservation of normal balance among usual members of physiologic flora [14].

Our Experience and New Problem

Our previous study [2] as well as the records of approximately 80,000 patients examined in our mycological laboratory, showed that in over 60% of cases there are positive findings of Candida in the stool samples. Nevertheless, the percentage of patients with Candida overgrowth (>10⁹ CFU/g of faeces) is significantly lower (8-10%). Interestingly, in a ten-year period, 2% of examined patients had positive findings of yeast overgrowth with causative species being Saccharomyces (S.) cerevisiae. This is a ubiquitous ascomycetous yeast that colonizes the respiratory, urinary and gastrointestinal tract of humans and is traditionally considered non-pathogenic. Recently, however, it has started to be considered as a potential pathogen and cause of superficial and invasive fungal infection. Accordingly, S. cerevisiae overgrowth on intestinal mucosa could be as problematic as Candida-overgrowth. On the other hand, S. cerevisiae-bulardi strain is a component of many probiotics and can quickly proliferate during prolonged treatment. In order to correctly interpret the findings of S. cerevisiae, we decided to have an interview with 100 patients. All of them, except one, stated that, according to physician recommendation, they have used probiotics that contain S. cerevisiae-bulardi strain for more than 20 days.

Besides previously stated problems that there is no general opinion about Candida-overgrowth on the intestinal mucosa and official guidelines regarding treatment and diet for this condition are lacking, additional problems are being recognized:

- Mycological analyses of the stool can suggest yeast overgrowth, yet it can be overgrowth of yeast from probiotics.
- In Serbia there are only a few microbiological laboratories equipped for mycological analysis and even fewer for differentiation of yeast strains.
- During the mycological analysis of the stool, overgrowth of Saccharomyces yeasts from probiotics can be easily mistaken for high counts of Candida spp. Therefore, only in case of macroscopic and microscopic examination, misinterpretation of result as Candida overgrowth may occur.
- Errors in result interpretation, as well as the fact that most physicians are neither familiar with the latest trends in mycology, nor with the risk that yeasts from probiotics can lead to Saccharomyces overgrowth on the intestinal mucosa, may subsequently mislead the doctor to start „treating the treatment“[15,16].

To conclude, it would be best to establish laboratory capacity for differentiation between Candida and Saccharomyces yeast; to implement purposeful education for both medical personnel and laymen which would enable regular patient follow-ups; and before mycological analysis of intestinal microbiota to obtained anamnestic data of each patient regarding disturbance of gastrointestinal tract and consumption of probiotics, as well as the duration of this kind of treatment. Finally, the most correct interpretation of mycological examination can be provided only by a multidisciplinary team and patient participation.
References