USE OF LACTOBACILLUS ACIDOPHILUS R0052 AND LACTOBACILLUS RHAMNOSUS R0011 PROBIOTIC STRAINS IN CHILDREN WITH BURN INJURIES

Summary. Today, burn injury is second most frequent diagnosis in all children hospitalized with injuries. The main cause of death in cases of extensive deep burns is burn infection that occurs in 23 to 82 % of all burn units’ patients. Antibacterial treatment rationality is of great importance in fighting the generalized infections. This paper is aimed at scrutinizing the incidence and course characteristics of the antibiotic-associated diarrhea (AAD) in burn patients, as well as the possibility of its prevention in children receiving antibacterial treatment in the Regional Burn Unit of Zaporizhzhia. During 2012–2015, we have observed 438 children with burn injuries, who received antibiotics. We observed children receiving antibiotics and examined over hospitalization time by detection of the highly specific for antibiotic-associated diarrhea A + B Clostridium difficile toxins in stool, which allowed diagnosing the enterocolitis due to Clostridium difficile associated with antibiotics administration (A4.07, ICD-10). AAD prevention methods have been developed, among which preventive (from the first hours of hospitalization) administration of oral probiotic agent containing Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 probiotic strains as a part of the Lacidofil® preparation dosed by age should be considered a major one. Prophylactic prescription of probiotic strains with antitoxic action against Clostridium difficile had reduced the incidence of antibiotic-associated diarrhea in children and the severity of its symptoms by 3.4 times.

Key words: children, burn injury, antibiotic-associated diarrhea, Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 probiotic strains.

Today, burn injury is second most frequent diagnosis in all children hospitalized with injuries. Burns remain among the most urgent and socially important issues of children’s traumatism. According to global statistics, 18 to 42 % of people suffer from burns of varying severity during their life [1]. Patients’ recovery and life prognosis depends on area and depth of the damaged skin. The development of burn disease is considered a dangerous condition for burned patients; the burn wound and resulting somatic changes cause adaptation mechanisms and body reactions stress, which might lead to death.

Burn shock, the first stage of the burn disease, can develop in children with burns of 5 to 10 % or more of the skin area, or with 3 to 5 % of damaged skin in cases of deep injuries. The peculiarity of children’s burn injury is associated with age-related anatomical and physiological characteristics. Due to helplessness, the child is subject to longer exposure during the damaging factor action, which leads to deeper burns, as compared with adults.
Loss of protective skin over a large area of the body surface creates conditions for microbial infestation on the one hand and disintegration of the major neurotrophic and metabolic functions of the organism on the other, which leads to disruption of anti-infective protection factors.The conditions(8,12),(989,982) for infectious process development and generalization are established in child’s body. Necrotic tissue formed in the area of burn injury is a favorable environment for the invasion and multiplication of microorganisms. The main cause of death in cases of extensive deep burns is burn infection that occurs in 23 to 82 % of all burn units’ patients [2, 3].

Prescription of antibiotics for patients with burns takes into account the surface area of damaged skin and stage of burn disease. For instance, if the area of burns is less than 10 %, the use of antibiotics is necessary with burdened pre-morbid background, specifically in patients with congenital heart disease, diabetes, hemoglobinopathy, renal diseases, or concurrent respiratory disease. In cases of burn area of 10 % or more, the antibiotic treatment is prescribed very frequently, usually on the background of thermal inhalation injury, in all cases of systemic inflammatory response, and against the threat of infection generalization. Any infectious process originating in the burn wound is able to trigger the development of severe complications, such as sepsis, pneumonia, septic arthritis, urinary tract infections, myocardiitis, and lymphadenitis. In order to prevent the emergence of infectious complications, antibiotic treatment is initiated during the burn shock period and continued against the background of anti-infective protection factors. The conditions for functions of the organism on the one hand, which leads to disruption of anti-infective protection factors. The conditions for functions of the organism on the other, which leads to disruption of anti-infective protection factors. The conditions for functions of the organism on the other, which leads to disruption of anti-infective protection factors. The conditions for functions of the organism on the other, which leads to disruption of anti-infective protection factors.

The lack of positive dynamics in the primary disease treatment and further development of complications, increase in systemic inflammatory response symptoms within 48 to 72 hours from the start of therapy, and the insensitivity of burn surface flora to administered antibacterial preparation requires antibiotic replacement. In severe disease course, combined antimicrobial treatment is used, which implies the simultaneous administration of two or even three preparations in their maximum therapeutic doses. It is clear that antibiotic treatment of many burn patients is characterized by high intensity and duration.

Under these conditions, the most important component of successful treatment is prevention of iatrogenic complications, particularly the antibiotic-associated diarrhea (AAD), which is unsafe for the patient’s life and able to develop on the background of any antibiotic therapy [4, 5].

This paper is aimed at scrutinizing the incidence and course characteristics of the AAD in burn patients, as well as the possibility of its prevention in children receiving antibacterial treatment in the Regional Burn Unit of Zaporizhzhia.

During 2012–2015, we have observed 438 children with burn injuries who received antibiotics in the Regional Burn Unit of Zaporizhzhia. Observations were divided into two stages.

During the first stage, in 2012–2013, we have observed 120 children receiving antibiotics and being examined over hospitalization time by detection of the highly specific for AAD A + B Clostridium difficile toxins in stool [6]. AAD has occurred in 32 (27 %) of 120 observed patients and was characterized by liquid stool (at least 3 times a day, usually 6 to 16 times) in at least 3 days after hospitalization and antibiotic preparations prescription, and persisted for at least 48 hours [7]. The children had pain along their large intestine and decreased appetite; the onset of disease was not accompanied by fever response and vomiting. The most frequent viral and bacterial causes of diarrhea, such as gastroenteritis, nutrition mistakes, laxatives, etc. have been excluded in these patients.

Among 32 samples of liquid stool taken from the patients with the aforesaid clinical picture, in 25 (78 %) Clostridium difficile toxins have been found, which allowed diagnosing the enterocolitis due to Clostridium difficile associated with antibiotics administration (A4.07, ICD-10) [8]. According to the clinical course, 12 of 32 patients had mild diarrhea, 10 children had AAD of moderate severity, and 10 had severe diarrhea that required additional rehydration fluid therapy [9].

We were not able to identify the priority effect of specific antibiotics on severity and incidence of AAD; however, effects of age (younger age group mostly), the degree of burn injury, and administration of antibiotics in combination have been observed. The results obtained allow us to conclude that AAD caused by antibiotic therapy is a significant problem for the children treated in the burn unit that needs to be addressed.

AAD prevention methods have been developed, among which preventive (from the first hours of hospitalization) administration of oral probiotic agent containing Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 probiotic strains as a part of Lacidifil® preparation dosed by age should be considered a major one. This probiotic agent had proved its effectiveness against antibiotic-associated diarrhea (including one associated with Clostridium difficile infection), being able to limit the pathogenic microorganisms’ intestinal colonization and block the entero-pathogenic (choleriform) and necrotic toxins [10–12]. In the subsequent period of 2014–2015, all 318 hospitalized patients have received antibiotics and their combinations similar to the previous ones in the same unit, which had not undergone any material or utility-related changes, except compulsory preventive therapy with Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 probiotic strains. At the same time, AAD has been diagnosed in 25 children (7.9 %) over the observation period. In order to treat AAD, Enterol® probiotic preparation based on Saccharomyces boulardii strain [13] has been administered to 20 patients; another 6 children required metronidazole as a specific antimicrobial agent [14, 15] at a dose of 30 mg/kg per day in 3 divided oral doses for a 5-day period.

Only one patient required additional rehydration therapy. It should be emphasized that while using Enterol® preparation, we sought to take all necessary precautions in
order to avoid any contact between the powder and wound surface. Therefore, an aqueous suspension of Enterol® sachet contents had been prepared in a separate room and then brought to the patient room for per os administration. Lacidofil® preparation does not require such precautions, as it is packed into capsules [16, 17]. In addition, no cases of human infection by Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 strains and occurrences of local or systemic infectious reactions have been registered over a long observation period [18–20]. It also should be noted that Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 probiotic strains administered to 318 children have not caused any side effects, or extended the terms of wound healing process, or formed any unusual manifestation of wound healing.

**Conclusions**

1. During 2012–2015, 438 children have been receiving antibiotic therapy of varying intensity in the Burn Unit; antibiotic-associated diarrhea of varying severity had developed in different observation periods in 7.9 to 27 % of children.

2. The majority of children (73 %) had antibiotic-associated diarrhea accompanied by the release of enteropathogenic toxins Clostridium difficile, spores of which are likely to constitute a normal microbial component of the Burn Unit contamination.

3. Prophylactic prescription of Lactobacillus acidophilus R0052 and Lactobacillus rhamnosus R0011 probiotic strains with antitoxic action against Clostridium difficile as a part of Lacidofil® preparation in patients receiving antimicrobial treatment had reduced the incidence of antibiotic-associated diarrhea in children and the severity of its symptoms by 3.4 times.

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Резюме. На сьогодні опіки посідають друге місце серед усіх травм дітей. Основною причиною летальних наслідків у випадку виразних та глибоких опіків є інфекція, що виникає у 23–82 % усіх випадків опіків. Раціональна антибактеріальна терапія має велике значення в боротьбі з генералізованою інфекцією. Метою цього дослідження було ретельне вивчення епідеміології та характеристики антибіотик-асоційованої діареї (ААД) у хворих дітей у опіках, а також можливість запобігання цій діареї, що виникала внаслідок антибактеріальної терапії в пацієнтів Обласного опікового відділення м. Запоріжжя. Про тиго 2012–2015 років ми спостерігали 438 дітей з опіковими травмами, які приймали антибактеріальні препарати.

Це дозволило діагностикувати Clostridium difficile-ентероколіт, пов’язаний з прийомом хворими антибіотиків (A4.07, МКБ-10). Використання пробіотичних штамів з антитоксичною активністю щодо Clostridium difficile скорочує в 3,4 раза число випадків антибіотик-асоційованої діареї у дітей з опіками та зменшує тяжкість її симптомів.

Ключові слова: діти, опікова травма, антибактеріальна терапія, антибіотик-асоційована діарея, пробіотичні штами Lactobacillus acidophilus R0052 та Lactobacillus rhamnosus R0011.