Clinical research

Borelis Pro phytomedicine for the complex treatment of Lyme borreliosis in children

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Abstract

Introduction: Lyme disease, also known as Lyme borreliosis (LB) (tick (Ixodes)borne borreliosis) is a transmissible, natural-focal disease characterized by damage of the skin, nervous system, heart.
Material and methods: Under observation were 68 children – residents of Ternopil region, who applied to Ternopil Regional Children Hospital, and whose age range was 8–17 years. Two schemes of complex treatment of patients were tested: the 1st – patients received Doxycycline (Unidox Solutab®), tablets 100 mg, 10 pcs. 2 time/day after meals for 14 days at a dose 4 mg/ kg; the 2nd – patients received the treatment regimen like the 1st group and phytomedicine "Boreliss pro" capsules, 28.56g, 60 pcs. (Duo Life Boreliss Pro., Poland) 1 capsule 2 time/day after meals for 14 days.
Results: Results showed that was significantly ($p < 0.05$) lower severity of LB in patients who received antibacterial therapy in combination with doxycycline hydrochloride and phytomedicine "Boreliss pro" (1 caps. 2 times/ day, after meals), compared with individuals in another group, on the 30th day after treatment. Complex therapy of patients by phytomedicine "Boreliss pro" causes a decrease of pro-inflammatory levels of cytokines IL-1β in the serum.
Conclusions: Comprehensive treatment of patients with an erythematous form of LB by phytomedicine "Boreliss pro" contributes to a significantly ($p < 0.05$) faster disappearance of clinical manifestations of LB, shortening the duration of doxycycline hydrochloride use, and reducing the likelihood of side effects from this drug.

Key words: Lyme borreliosis, doxycycline hydrochloride, Boreliss pro.

Introduction

Lyme disease, also known as Lyme borreliosis (LB) (tick (*Ixodes*)-borne borreliosis), is a transmissible, natural-focal disease characterized by damage to the skin, nervous system, and heart, and it often takes a chronic, recurrent course [1, 2].

Several types of pathogenic microorganisms – *Borrelia burgdorferi*, *Borrelia garinii*, *Borrelia afzelii*, *Borrelia spielmanii*, and *Borrelia bavariensis* – are considered to be the causative agents of LB and the cause of most cases of LB in Europe.

The available treatment methods for infectious diseases, including LB, are based on using medicinal plants, their mixtures and herbal medicinal products [3]. A herbal formulation called *Borelis pro* contains several medicinal plants: *Cistus incanus* L., root extracts of *Dipsacus sylvestris*, flavonoids and BAS of garlic (*Allium sativum* L.) and oregano (*Origanum vulgare* L.), *Polygonum cuspidatum* Siebold & Zucc. Biologically active compounds (BAC) of these plants determine the pharmacological effect of Borelis pro.

Cistus incanus L. contains several polyphenolic compounds, in particular flavonoids and tannins, which have pronounced antioxidant properties and immune-stimulating effects [4]. Evidence suggests [5] that various cytokines participate in the development of the immune response to the entry of an antigen into the body.

IL-1β is viewed as a key mediator of the inflammatory response to pathogens. Specifically, it plays a significant role in the development of the response to acute tissue damage and disease chronicity [5]. It may be surprising that there is great interest in whether this protein is produced in Lyme borreliosis, given that the disease has a pronounced tendency to chronicity [6].

The goal of the study is to evaluate the efficacy of the pharmaceutical *Borelis pro* to treat children with LB.

Material and methods

We observed patients with tick bites. Our study included 68 children, aged between 8 and 17, based in the Ternopil region, Ukraine. The studied group with clinical symptoms of LB and antibodies to specific proteins of B. *burgdorferi* antigen included 68 persons. The diagnosis of ring-shaped erythema migrans (EM) was established clinically based on characteristic manifestations and epidemiological history. Blood sampling was performed twice – before (sample 1) and after antibiotic therapy (sample 2). A total of 68 children were examined: 16 children with erythema migrans and arthritis, 26 children with non-erythematous form.

The complex treatment of patients with an erythematous form of LB was performed according to the following schemes: Group 1. The patients received doxycycline (Unidox Solutab), tablets 100 mg, 10 pcs. (Astellas Pharma Europe, B.V., The Netherlands) 2 times/day after meals for 14 days at a dose of 4 mg/kg. Group 2. The patients received doxycycline hydrochloride plus the herbal formulation Borelis pro, the same treatment regi-

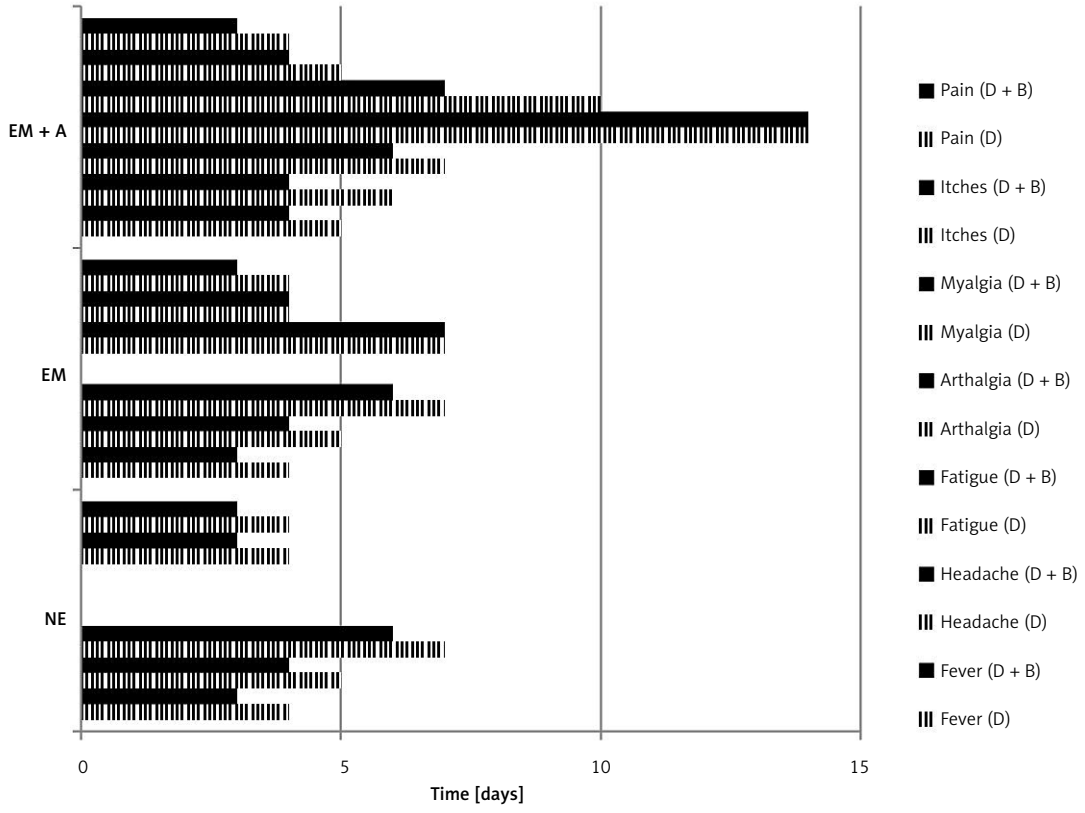

Figure 1. Dynamics of clinical symptoms

men as Group 1 and *Borelis pro* capsules, 28.56 g, 60 pcs. (Duo Life Boreliss Pro S.A., Poland) 1 capsule 2 times/day after meals for 14 days. There were 38 children in this group.

The effectiveness of treatment was assessed based on the dynamics of clinical manifestations of the disease and the level of cytokines: pro-inflammatory – interleukin IL-1β and anti-inflammatory – interleukin IL-10 in the serum of patients [7, 8]. IL-1β and IL-10 were studied twice – before treatment and after (on the 14th day).

The levels of cytokines IL-1β and IL-10 in the serum of patients were determined with ELISA test systems (CJSC Vector Best). The following concentrations were considered as reference values: for IL-1β – up to 11 pg/ml, for IL-10 – up to 31 pg/ml.

Statistical analysis

A statistical analysis of the results was conducted using the methods of parametric and nonparametric statistics – Microsoft Office Excel, Statistica and Mann-Whitney *U*-test statistics. Conclusion of the Commission on Bioethics of I. Horbachevsky Ternopil State Medical University, Ministry of Health of Ukraine, dated 1st of November, 2021 (protocol No. 66).

Results

The mean interval between the tick bite and clinical symptoms was 12 days, followed by a 14-day interval before clinical diagnosis and treatment (2–31 days).

EM was observed in 14 (31.9%) patients within 24 h. In 13 (29.5%) patients the appearance of EM was observed after 24–48 h and in 2 (4.5%) children on the 3rd day; in 1 (2.3%) patient EM was found after a few months.

Patients in the first group had arthritis syndrome, which occurred 1 month after a tick bite with manifestations of ME (Figure 1).

The clinical symptoms tended to regress with the use of complex treatment.

The serum concentration of the anti-inflammatory interleukin IL-10 was the lowest before treatment in patients with erythematous LB. It did not differ from the control group (CG) (Table I). The concentration of the interleukin IL-10 in patients with EM and EM in combination with arthritis was slightly higher than in the CG. The increased level of the anti-inflammatory cytokine IL-10 in patients with EM can be considered as a protective response to inhibit the activity of pro-inflammatory cytokines [7, 8].

After treatment with both doxycycline hydrochloride and complex antibiotic + herbal formulation *Borelis pro* there was an increase in interleukin IL-10, but in combination treatment, this figure was much higher (Table I). This indicates

Table I. Level of interleukins IL-1 and IL-10

Index	Normal [pg/ml]	EM + arthritis (*n* = 16)				EM (*n* = 26)				NE (*n* = 26)			
		Before treatment	After treatment			Before treatment	After treatment			Before treatment	After treatment		
			10	6			10	16			10	16	
			DH	DH + Bp			DH	DH + Bp			DH	DH + Bp	
IL-1β	0–11	4.8 ±0.2*	2.5 ±0.2*/#	2.3 ±0.1*/#		3.0 ±0.3*	1.9 ±0.1*/#EM	1.4 ±0.1*/#EM		1.9 ±0.1	1.9 ±0.1	1.4 ±0.1*/#NE	
IL-10	0–31	9.0 ±0.5*	12.8 ±0.4*/#	16.9 ±0.2*/#		7.5 ±0.3*	16.6 ±0.1*/#EM	17.6 ±0.2*/#EM		4.0 ±0.2*	7.9 ±0.3*/#NE	8.5 ±0.4*/#NE	

**p < 0.05 There was significantly (p < 0.05) lower severity of LB in children who received Borelis pro in the complex with doxycycline hydrochloride at a dose of 4 mg/kg on the 14th day after the end of treatment than in those who received only antibiotic therapy.*

that the biologically active compounds (BAC) show pronounced anti-inflammatory and antioxidant activity.

Discussion

We assume that the reduction of LB manifestations is due to a complex of BAC of plant origin that are part of *Borelis pro*, and which have pronounced antioxidant, antiviral, immune-stimulating, and anti-inflammatory properties.

BAC can also reduce the toxic effects of antibiotics on the body, promote the formation of cellular and humoral immunity and accelerate the patient's recovery [9].

The usage of phenolic compounds in treatment is very promising since natural antioxidants easily and organically enter the metabolic processes in the body and have virtually no side effects [10, 11].

We found that *Borelis pro* has a positive effect on the course of LB, improve patients' condition and promotes their recovery. A range of criteria for assessing the disease was established in the first phase of research given that Lyme disease is a polysystemic disease with a polymorphic clinical picture. However, the interleukins IL-1 and IL-10 cannot be traced to the dynamics of the disease. It also prevents complications of the cardiovascular, urinary and gastrointestinal systems [12, 13].

Due to the complexity of *Borrelia* cultivation, it is considered unjustified to research the phagocytic response to them. An assessment of the NF-κB-mediated pathway in the development of borreliosis and T cell activation will be undertaken in further studies, as this was not the purpose of the present study [14].

It improves the overreaction of Th1 and CD8+ T cells, which are characterized by excess production of IFN-γ and TNF-α and are also responsible for immune pathology associated with many infections, including toxoplasmosis, trypanosomiasis, malaria, and mycobacteriosis. In collaboration with Th1 cytokines (such as IL-12), it regulates Th2 responses [8, 9, 18–20], and prevents the overproduction of IL-4, IL-5 and IL-13 [15].

Taking into account the investigation of this interleukin the data are scarce, further development of criteria for the diagnosis of Lyme borreliosis seems to be promising.

In conclusion, the use of doxycycline hydrochloride in the complex treatment of patients with LB together with *Borelis pro* contributes to significantly fast disappearance of clinical manifestations of the disease and reduces the likelihood of side effects caused by antibiotic therapy. Complex therapy with *Borelis pro* reduces the level of proinflammatory IL-1β in the serum and increases the concentration of anti-inflammatory IL-10 and the development of cellular and humoral immunity, which eliminates *Borrelia* and speeds up recovery.

Conflict of interest

The authors declare no conflict of interest.

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