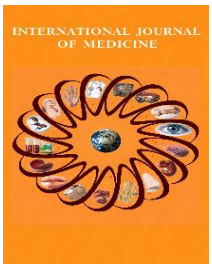

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Brief Report

The impact of probiotic bacteria on *Helicobacter pylori*

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Abstract

The prevalence of *Helicobacter pylori (H. pylori)* infection is 22-95% in the developing countries and 1-58% in the developed. It varies by geographic location, ethnicity, socioeconomic status, and age. *H. pylori* is considered an etiologic factor for the development of multiple conditions like peptic ulcer disease, gastric adenocarcinoma, and MALT lymphoma and possibly type 2 diabetes mellitus, chronic obstructive bronchitis, acute coronary disease, end-stage renal disease. The recommended treatment regimen for *H. pylori* is the standard triple therapy with a proton pump inhibitor (or ranitidine, bismuth citrate), with clarithromycin and amoxicillin or metronidazole. Nevertheless, since the 90's the eradication rate of these triple regimens has decreased from 90% to 70%, due to *H. pylori* resistance to key antibiotics, mainly clarithromycin, but also metronidazole and levofloxacin. In two series of experiments, the effect of bacteria of *H. pylori* on the body's health was studied against the background of the targeted use of microorganisms with probiotic potential.

Keywords: bifidobacterium; Helicobacter pylori; lactobacillus; probiotics

1. Introduction

The prevalence of *Helicobacter pylori* (*H. pylori*) infection is 22-95% in the developing countries and 1-58% in the developed. It varies by geographic location, ethnicity, socioeconomic status, and age [1]. Despite the modern treatment possibilities, the recurrence rate is 1.75-3.25% and the annual reinfection rate can be up to 13% [2-4]. Therefore, it is still a necessity to improve the treatment and prophylaxis regimens for this group of patients. Moreover, current treatment regiments are far from optimal. Due to the increase in the prevalence of *H. pylori* resistance to antibiotics, triple therapy with clarithromycin is no longer the best treatment regimen for H. pylori, since in some areas the resistance to this antibiotic is higher than 20% [5].

There is data that probiotics containing bifidobacteria and/or lactobacteria can affect the multiplication process of *H. pylori* in the digestive tract as well as improve the treatment course [2-4,6-8].

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It was demonstrated that children's intestinal microflora can change its properties in the presence of lactoferrin and probiotics, thus demonstrating the rationality of using complex therapy in the case of *H. pylori* [9]. Other studies demonstrate that in the presence of probiotics the efficiency of anti-helicobacter treatment is increased along with a decrease of possible side effects of the treatment [10,11]. Therefore, the aim of this work was to study the impact of different bacterial species (of genus-specific for the *Lactobacillus* digestive tract or in association with *Bifidobacterium*) on *H. pylori* in mice.

2. Methods

Two series of experiments were performed on laboratory animals (white mice). There were three series of laboratory animals, i n each series there were three groups of animals, in each group ten mice.

The first series was designed to study the process of reproduction of certain genes of microorganisms in the digestive tract and the introduction of a suspension of lactobacilli. The same process was compared for animals that did not receive a suspension. Lactobacillus was administered orally (1 billion microbial cells suspended in 1 ml of saline for 10 days during the day).

In the second series, we also administered *H. pylori*, 1 million microbial cells per animal. This dose was administered orally only once based on the final background of lactobacilli in the intestinal contents (optimal or non-optimal).

Both, the first and second groups were tested while the third one was a control group. Samples of intestinal contents were collected at the beginning and end of the experiments (it was decimally diluted to 10^{-9}).

During the experiments, we used *H. pylori* strain CIP 103995 (identical to ATCC 43504) was obtained from Centre de Resources Biologiques de l'Institut Pasteur, France.

The research process included several stages: replacement of diluted samples on agar nutrient media for each microorganism (*Bifidobacterium, Lactobacillus, Escherichia, Proteus*, and *Enterococcus*) by Himedia incubation at (37±1) °C. We counted grown colonies on selective agar culture media, multiplying the obtained colonies by the studied dilution and the decimal logarithm of the final number. The calculation of the results was carried out by determining the quantitative indicators of microorganisms of the named genres, expressed in decimal logarithm (log).

This study was conducted in accordance with the declaration of Helsinki. The experiments were carried out according to the ethical standards and approved by the ethical committee of the State Medical and Pharmaceutical University "N.Testemitanu".

3. Results

The results obtained at the end of the first series of the numerical value level of microorganisms from the genus: *Bifidobacterium, Lactobacillus, Escherichia, Proteus,* and *Enterococcus* are presented in table 1.

The results demonstrate that the lactobacilli have reached the optimal level by their coordinated administration. At the end of the first series lactobacilli in experimental series, I and II constituted respectively 9,5+0,15 and 9,94+0,14 log/g or by 72,20% and 69,46% more than from the start.

At the same time, the quantitative indices of lactobacilli were 5,38+0,13 log/g, and the dynamics of growth was only 2,24%. Achieving the optimal level of lactobacilli in intestinal content has also contributed to the change in bacteria quantity of other genres. For example: the number of Bifidobacterium compared to the initial number has increased by 97,32 and 96,47%, but for *Escherichia, Proteus*, and *Enterococcus* the number of which has decreased.

The abovementioned results demonstrate that in the experimental groups at the end of the experiments in the first series the microbial balance between the gender of microorganisms and the quantitative level of each of them was relatively optimal.

That was the point when the animals were administered microbial suspension of *H. pylori* (II series).

We observed the animals for 10 days after the administration of the *H. pylori* suspension. The animals haven't shown symptoms of infection. The group of animals that were subjected to the experiment did not die. At the same time in the control group, 30% of mice died.

4. Discussion

H. pylori is considered an etiologic factor for the development of multiple conditions like peptic ulcer disease, gastric adenocarcinoma, and MALT lymphoma and possibly type 2 diabetes mellitus, chronic obstructive bronchitis, acute coronary disease, end-stage renal disease [12,13].

It is known that *H. pylori* microorganisms are a danger to human health in particular conditions. In biological experiments, it has been demonstrated that this danger was found to be directly dependent on the existing microbial background of the gastrointestinal tract. For example: if the causative agent encounters intestinal equilibrium, then the inflammatory or infections process may not develop [14,15].

Table 1. The quantitative indices of genes of intestinal microorganisms on laboratory animals (white mice) that received and didn't receive the selected experimental native bifidobacterium

The batch of animals	The genus of microorganisms	The quantity of microbial cells per 1 gr of intestinal content, decimal logarithms (log)		The difference compared to the initial level	
		Time during research			
		Initial	Final	Log	%
I	1	4.49+0.11	8.86+0.13	4.37	<97.32
	2	5.54+0.12	9.54+0.15	4.00	<72.20
	3	9.14+0.14	6.20+0.12	2.94	>32.16
	4	6.20+0.13	2.07+0.08	-4.13	>66.61
	5	9.65+0.10	5.41+0.11	-4.24	>43.93
II	1	4.54+0.14	8.92+0.15	4.38	<96.47
	2	5.60+0.15	9.49+0.14	3.89	<69.46
	3	9.32+0.11	6.30+0.12	-3.02	>32.40
	4	6.41+0.12	3.17+0.09	-3.24	>50.54
	5	9.77+0.13	5.65+0.13	-4.12	>42.16
III	1	4.49+0.13	4.60+0.11	0.11	<2.44
	2	5.32+0.14	5.38+0.13	0.06	<1.12
	3	8.80+0.15	8.92+0.15	0.12	>1.36
	4	6.04+0.10	6.13+0.12	0.09	>1.49
	5	9.53+0.16	9.62+0.14	0.09	>0.94

Animal series: I and II-experimental; III-control. The genres of micro-organisms: 1.-*Bifidobacterium*, 2.-*Lactobacillus*, 3.-*Escherichia*, 3.-*Proteus,* and 5.-*Enterococcus*.

The recommended treatment regimen for *H. pylori* is the standard triple therapy with a proton pump inhibitor (or ranitidine, bismuth citrate), with clarithromycin and amoxicillin or metronidazole [16]. Nevertheless, since the 90's the eradication rate of the triple regiment has decreased from 90% to 70%, due to *H. pylori* resistance to key antibiotics (mainly clarithromycin, but also metronidazole and levofloxacin) [17,18]. Taking into account these obstacles new treatment options are currently at special attention.

Probiotics are live microorganisms, which in adequate amounts have a health benefit on the host. The most used probiotic bacteria are *Lactobacillus* and *Bifidobacterium* [19]. It was demonstrated that probiotics could improve *H. pylori* eradication and reduce side effects during therapy [20]. Nevertheless, some authors warn that gastrointestinal colonization with helicobacter alters the effect of probiotics [21]. A recent systematic review demonstrated that probiotics alone show a minimal effect on *H. pylori* clearance, thus demonstrating their direct role (with a mean eradication rate of 14%) [22]. This may be due to the effect of certain immunological (modulation of anti-inflammatory cytokines secretion) and non-immunological (production of antimicrobial substances competing with *H. pylori* for adhesion receptors, stimulating mucin production and stabilizing the gut mucosal barrier) mechanisms [5].

In our research, two series of experiments were carried out to evaluate the effect of probiotics on *H. pylori*. It was established that the initial administration of such bacteria to the laboratory animals in the tested dose prevents the development of the infectious process.

4.1. Conclusion

In order to avoid the development of intestinal pathology caused by *H. pylori*, we consider that bacteria strains marketed as probiotics can be an option for treatment. Probiotics can help to reach the microbial balance or optimal level of each bacterial species. In such a case there would be a lower chance for the development of infection with *H. pylori*. Therefore, *H. pylori* is less harmful in the case of balanced intestinal flora at the quantitative optimal level.

Conflict of interest

The authors declare that they have no conflict of interest.

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