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*The role of pro-inflammatory interleukin-1 β during stress-induced
injury without/with microbiota variation*

Rola prozapalnej interleukiny-1 β w uszkodzeniu indukowanym stresem bez oraz ze zmianami
mikrobiotycznymi

INTRODUCTION

In our previous research it was shown that in rats water immersion restraint stress (WRS) according to Takagi et al. evoked non-erosive injuries of mucous coat of esophagus, which were the most pronounced in 48 hours after stress action. The use of multiprobiotic “Symbiter® acidophilic concentrated” (Symbiter) accelerated restorative regenerative processes in the mucous coat of esophagus [10]. Taking into account the known facts that in rats stress of any duration increases blood serum level of proinflammatory cytokine interleukin-1 β (IL-1 β) [7] and immune activation evoked by stress may also contribute to affective illness [1], the aim of our work was to investigate the stress influence on IL-1 β level in blood serum in different period after stress and its possible correction by Symbiter.

MATERIAL AND METHODS

The study was carried out on 42 white rats. The animals were deprived of food for 24 hr prior the experiments with an easy approach to water. They were divided into six groups. The animals of the first group were intact control. The rats of II–VI groups were subjected to WRS according to Takagi et al. [1964]. Blood sampling in rats for test IL-1 β level was accomplished in 5 minutes (II group), in 24 hours (III and IV groups) and in 48 hours (V and VI groups). The rats of III and V groups twice a day were injected placebo (0.5 ml of tap water per os). The rats of IV and VI groups twice a day were injected Symbiter (0.5 ml water 140 mg/kg dissolved in 0.5 ml water). Symbiter (limited company «O.D.Prolisok») is concentrated fluid biomass of bioplasts of symbiosis of 14 microorganisms strains. The composition of one dose (10 ml) of Symbiter is concentrated biomass

of bioplasts of bacterium symbiosis CFU/cm³, no less: Lactobacillus and Lactococcus – 6.0×10^{10} , Propionic bacterium – 3.0×10^{10} , Bifidobacterium – 1.0×10^{10} , Acetic bacterium – 1.0×10^6 . The level of IL-1 β in blood serum was the evaluated using the method of enzymeimmunoassay with the help of a commercial kit produced by GE Healthcare (Amersham IL-1 β Rat Biotrak ELISA System).

The statistical processing of data was carried out in the package of software “Statistica 6.0”. Results are expressed as the mean $\pm$ SD. Using Shapiro-Wilks’ W test it was found out that data were normally distributed. Therefore, statistical comparisons between groups were conducted using the Student’s t-test for independent samples. Statistical significance was accepted with a $p < 0.05$.

RESULTS

In the rats of control group blood serum level of IL-1 β was 314 ± 158 pg/ml. Within 5 minutes after completion of WRS action expression of IL-1 β in blood serum increased by 28% ($p < 0.05$). 24 and 48 hours after completion of WRS action expression of IL-1 β in the blood serum increased by 43% ($p < 0.05$) and 79% ($p < 0.001$), respectively. Taking into account our previous data that in rats WRS evoked the most pronounced non-erosive damages of the mucous coat of esophagus in 48 hours after stress action [10] we concluded that the development of non-erosive injuries of mucous coat of esophagus correlates with the increase in the level of proinflammatory cytokine IL-1 β in blood serum. The immunostimulatory effect of normal flora and probiotics is a well-established fact [5]. That is why the effect of Symbiter on the decrease of the level of IL-1 β in blood serum and as a result of its positive effect on healing of non-erosive damages of mucous coat of esophagus is not surprising.

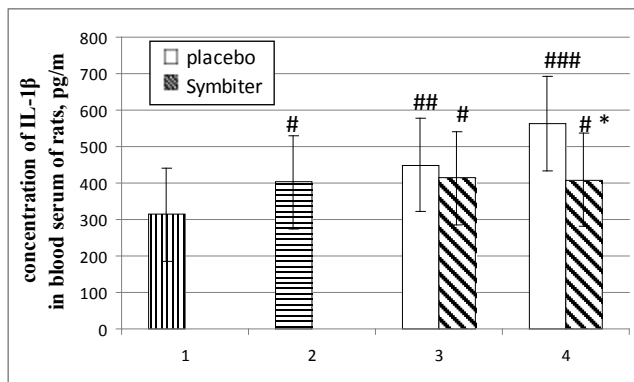


Fig. 1. The influence of multiprobiotic “Symbiter” on the content of IL-1 β in blood serum of rats after water immersion restraint stress (WIRS) ($M \pm SD$); 1 – control (intact rats) ($n=10$), 2 – 5 min after WIRS ($n=10$), 3 – 24 h after WIRS ($n=20$), 4 – 48 h after WIRS ($n=20$); * $p < 0.05$ compared with rats, that were given water during the same time, # $p < 0.05$ compared with intact rats, ## $p < 0.01$ compared with intact rats, ### $p < 0.001$ compared with intact rats

DISCUSSION

WRS evoked response of the immune system. As a result, the level of IL-1 β in the blood serum was increased within 5 minutes, 24 and 48 hours after completion of WRS action. This is consistent with the literature data that the stress of any duration and intensity causes increase in the level of IL-1 in the blood serum [7]. It is known that IL-1 reinforces activation of hypothalamic-pituitary-adrenal axis which in turn leads to an increased level of corticosteroids in the blood [2, 3, 9]. Corticosteroid hormones decrease secretion of gastric mucus and also diminish the content of sialic acid in gastric mucus [6, 8] and thus lead to the defeat of the protective mucous barrier. In addition, corticosteroids violate the regeneration of the epithelial cells of the gastrointestinal tract and enhance the formation of histamine from histidine. Corticosteroids disrupt the microcirculation, causing ischemia of the gastric mucosa. Taking into account the data obtained by Chen et al. [4] that probiotics have properties to decrease the level of IL-1 in blood serum in conditions of experimental colitis we concluded that the therapeutic effect of Symbiter on non-erosive damages of the mucous coat of esophagus is due to its impact on the level of IL-1 β in the blood serum as well as indirect effect on lowering the secretion of corticosteroids.

CONCLUSIONS

Water immersion restraint stress evoked response of the immune system. As a result, the level of proinflammatory cytokine IL-1 β in the blood serum increased. Injection of multiprobiotic Symbiter to rats after stress action decreases the level of IL-1 β in the blood serum indicated that it may be one of the mechanisms of protective action of Symbiter to stress-evoked injuries in mucosa of the gastrointestinal tract.

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SUMMARY

Water immersion restraint stress according to Takagi et al. evoked activation of the immune system in rats, which was manifested in an increase of interleukin-1 β level in blood serum within 5 minutes, 24 and 48 hours after completion of the stress action. The largest increase was observed after 48 hours. The injection of multiprobiotic *Symbiter® acidophilic concentrated* to the rats twice a day after the stress led to a decrease in the level of interleukin-1 β in the serum after 24 hours and its normalization after 48 hours after stress action.

Keywords: stress, interleukin-1 β , microbiota, multiprobiotic.

STRESZCZENIE

Zastosowanie u szczurów wodnego zanurzeniowego stresu immobilizacyjnego wg Takagi i wsp. powodowało aktywację systemu immunologicznego, co manifestowało się wzrostem stężenia interleukiny-1 β w 5 minucie, 24 i 48 godzinie po zakończeniu testu. Największy wzrost zaobserwowano w 48 godzinie. Podanie szczurom po stresie dwa razy dziennie multiprobiotyku *Symbiter® acidophilic concentrated* prowadziło do spadku poziomu interleukiny-1 β w surowicy po 24 godzinach i jej normalizacji po 48 godzinach od zadziałania stresu.

Słowa kluczowe: stres, interleukin-1 β , mikroflora, multiprobiotyki