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The use of complex therapy in experimental pyoinflammatory infection caused by *K.pneumoniae*

Background. Encapsulated *Klebsiella pneumoniae* has emerged as one of the most clinically relevant and more frequently encountered opportunistic pathogens as can cause a wide range of nosocomial infections, including pneumonia, bacteremia, and urinary tract infections[1] in host with weakened immune systems[2]. And also is one of the most frequently isolated pathogens from intensive care unit patients and is responsible for approximately 15% of the Gram-negative infections[3]. Clinical data indicate *K. pneumoniae as* one of the top four organisms recovered from the blood of burn patients involved in combat operations overseas[4]. Many of these *K. pneumoniae* clinical isolates are highly resistant to commonly used antibiotics, resulting in increased mortality[5].

The aim of the study was to improve the effectiveness of therapy of inflammatory processes caused by *K.pneumoniae.*

Methods. Clinical strains were isolated from specimen according conventional methods followed by identifying in ENTEROTEST-24 kits (Laxema, Czech republic). After checking the sensitivity of *K.pneumoniae* isolated strains to antimicrobial agents for research were selected amikacin and cefperazon/sulbactam, *in vivo* these antimicrobial agents were used in combination with immunomodulators "Ronkoleukinum" and "Glutaxim". Adapted for *K.pneumoniae* experimental model of inflammatory infection was obtained in mice, male, line C57BL/J6Sto[6].

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Work with laboratory animals was carried out under the European Convention. Daily doses of drugs were calculated on the basis of specific factor[1]. The content of cytokines was determined using ELISA kits according to instructions. Immune cells were determined using monoclonal antibodies of firm Serotec. Statistical analysis of data was performed using the program Biostat.

Results. It was revealed that the mortality of laboratory animals infected by *K.pneumoniae* varied depending on provided therapy. Under treatment only with amikacin mortality rate was reduced in 2 times and was 25 % compared with infected group without antimicrobial therapy. Using only cefperazon/sulbactam resulted in mortality of 35 %. Combination of amikacin with cefperazon/sulbactam decreased mortality rate to 40 %. The data according mortality of laboratory animals under using only of antimicrobial drugs showed that such therapy was not so effective, and also it was confirmed by analysis of changes in the immune system of laboratory animals. So, the next stage of experimental research was the development of effective schemes of complex use of antimicrobial therapy with immunomodulators. In group 1 laboratory animals were treated with amikacin, cefperazon/sulbactam in combination with Ronkoleukinum; in group 2 the same antibiotics were used together with Glutaxim. In addition to antibiotic therapy using of Ronkoleukinum and Glutaxim significantly decreased mortality rate in comparison with the infected group from 50 % to 0 %. So, combination of antibiotic therapy with immunomodulators reduced mortality in group 1 to 5 % and directly to 0 % in group 2. Under combination of antimicrobial and immunomodulators restoring of the immune system was detected. Thus, in group 1 the parameters of immune system (CD3+ 59,7±2,4 %, CD4+ 31,6±1,9 %, CD8+ 33,2±1,6 %, CD16+ 19,8±1,2 %) were near to indexes of the intact group (CD3+ 67,5±2,9 %, CD4+ 39,1±1,9 %, CD8+ 28,8±1,8%, CD16+ 12,9±1.1 %). In group 2 the complex treatment led to normalizing of the immune parameters (CD3+ 66,8±2,2 %, CD4+ 38,7±1,4 %, CD8+ 29,1±1,3 %, CD16+ 13,4±1,1 %).

Comparison of cytokine state in mentioned groups with control groups revealed significant effects of immunomodulators, namely results in reducing the amount of pro-inflammatory cytokines (IL-17 and IL-18). In group 1 concentration of IL-17 was corresponded to the level of intact animals (1,42±0,4 pg/ml), and the level of IL-18 decreased in 10,1 times (9,16±0,8 pg/ml) compared with the rate of IL-18 in infected group, but was in 1,8 times higher than index of intact animals. In group 2 the level of pro-inflammatory cytokines was significantly reduced ($p < 0,001$), IL-17 in 134 times (0,62±0,08 pg/ml) and IL-18 in 38,6 times (2,4±0,9 pg/ml) compared with infected animals.

Conclusions. Thus, the use of immunomodulator Glutaxim helps to restore immune state that allows recommending it in treatment of inflammatory processes caused by *K.pneumoniae*.

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