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10-15

MICROORGANISMS ANTIBIOTIC SENSITIVITY DETERMINATION IN URINARY TRACT INFECTIONS

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Introduction. Nowadays Urinary tract infections (UTI) are considered to be the most common bacterial infections. *Escherichia coli* is the most frequently uropathogen. Other microorganisms of the genera *Enterococcus*, *Klebsiella*, *Enterobacter*, *Proteus*, *Morganella*, *Citrobacter*, *Serratia*, *Pseudomonas*, *Streptococcus*, *Staphylococcus*, *Candida* are also isolated with variable frequency. In recent years there has been a decreasing tendency of the causative agents of UTI sensitivity to various antibiotics, which causes growth of an inefficiency treatment risk. In connection with the above the investigations were carried out with the purpose to identify the actual causative agents of bacteriuria and their sensitivity to antibiotics and antifungal drugs. **Materials and methods.** Bacteriological examination of urine was performed at 42 patients of SI "Sytenko Institute of Spine and Joint Pathology, AMS of Ukraine" clinic. The bacteriological method for determining the number of bacteria in the test material, cultural and bacterioscopic methods for identifying microorganisms and disk-diffusion method for sensitivity of microorganisms to antibiotics determining were used. The clinical material for the study was an average portion of the morning urine or urine collected by catheter. The biological material collection and bacteriological examination was carried by quantitative method, the isolated microorganisms identification and their sensitivity to antibiotics determining was performed by standard methods in accordance with current guidelines. We used the following antibiotics group to determine the microorganisms sensitivity: penicillin, cephalosporin, karbapenems, tetracyclines, aminoglycoside, fluoroquinolones, oxazolidinones, macrolides, lincosamides, glycopeptides, antifungal antibiotics. **Results and discussion.** During the biological material study 55 isolates of bacterial and fungal pathogens were obtained. The microorganisms' concentration in urine was in the range of $3,0 \times 10^6$ CFU/ml to $3,0 \times 10^9$ CFU/ml, and the most bacterial isolates content was equal $1,5 \times 10^9$ CFU/ml. Among the most commonly identified microorganisms *Escherichia coli* and *Staphylococcus spp.* were often detected in $5,3 \times 10^8$ CFU/ml concentrations. For *Streptococcus spp.* and *Proteus mirabilis* that value was $1,5 \times 10^9$ CFU/ml; for *Klebsiella pneumoniae* - $3,0 \times 10^8$ CFU/ml; for *Candida spp.* - $3,0 \times 10^6$ CFU/ml respectively. The most common microorganisms (which frequency of occurrence in urine was $\geq 5\%$) were: *E. coli* (14,5 \pm 4,7)%, *Str. agalactiae* and *St. haemolyticus* (10,9 \pm 4,2)%; *St. aureus* and *Pr. mirabilis* (7,3 \pm 3,5)%; *St. epidermidis*, *Kl. pneumoniae*, *St. hominis*, *Candida spp.* (5,4 \pm 3,0)%. While analyzing obtained results we concluded that meropenem was the most effective drug, 78,7% of all cultures had the sensitivity to it. The sensitivity to gatifloxacin had 73,7% of cultures; to tigecycline - 71,1% of isolates; to amikacin - 67,3% of cultures; to moxifloxacin - 59,6% of isolates; to two drugs (levofloxacin and pefloxacin) - 55,8% of isolates respectively. It was found that *Staphylococcus aureus* appeared to be resistant to vancomycin, ampicillin, cefuroxime, cefazolin, azithromycin, linezolid. This species and *St. epidermidis* and *St. hominis* isolates were multi-drug resistant to four or more drugs from different groups. All *Streptococcus agalactiae* isolates were insensitive to cefuroxime. All *Escherichia* cultures were resistant to cefuroxime, *Proteus* - to cefuroxime, ampicillin and cefazolin. *E. coli*, *Pr. mirabilis*, *K. pneumoniae*, *Ps. aeruginosa*, *Ac. haemolyticus* had multi-drug resistance. In addition, (73,1 \pm 6,1)% of all 52 bacterial isolates obtained were resistant to amoxiclav. **Conclusions. 1.** The most common microorganisms (which incidence in urine were $\geq 5\%$) are: *Escherichia coli* (14,5 \pm 4,7)%, *Streptococcus agalactiae* and *Staphylococcus haemolyticus* (10,9 \pm 4,2)%; *Staphylococcus aureus* and *Proteus mirabilis* (7,3 \pm 3,5)%; *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, *Staphylococcus hominis*, *Candida spp.* (5,4 \pm 3,0)%. **2.** The most effective antibacterial drug is meropenem. 78,7% of all isolates have sensitivity to it. The sensitivity to gatifloxacin have 73,7%; to tigecycline 71,1%; to amikacin - 67,3%, to moxifloxacin - 59,6% of cultures, to two agents (levofloxacin and pefloxacin) - 55,8% of cultures respectively. **3.** 100% of the family *Micrococcaceae* isolates were resistant to benzylpenicillin, 95,8% - to ampicillin, 87,5% - to amoxicillin and cefuroxime, 83,3% - to azithromycin, erythromycin and lincomycin. Members of the *Streptococcaceae* family were resistant to cefuroxime. 100% of the family *Enterobacteriaceae* isolates had no sensitivity to carbenicillin, 87,5% of isolates - to cefuroxim and gentamicin, 81,2% - to amoxicillin and ampicillin, 75,0% - to cefazolin, 50,0% - to ceftriaxone and aztreonam. **4.** *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis* *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter haemolyticus* isolates were multi-drug resistant.

DEPENDENCE BETWEEN ACYLATION DEGREE AND SPECIFIC LYSIS ACTIVITY OF THE PSEUDOMONAS AERUGINOSA M6 BACTERIOPHAGE

16-20

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Introduction. The purpose of this work is to study the influence of various degrees of protein's acylation on lytic activity and other biological properties of *Pseudomonas* M6 bacteriophage. **Materials and methods.** The subject of the study were samples of the *Pseudomonas* O 12 bacteriophage, hereinafter named the M6 phage. Pure phage lines were obtained from individual standard-morphology phage plaques (plaque-forming units, or PFUs) after ten passes over the indicator strain. In subsequent experiments, M6 phage samples were selected that had a sufficient level of purity (homogeneous in the morphology of virions that inactivated the homologous antiphage serum by no less than 99.0% and the heterologic antibacterial serum by no more than 1%), and a titer no lower than

10 PFU per ml (PFU/ml). Titration of the phages was conducted using the standard bilayer agar. The crude protein content in the phage suspensions was determined using the spectroscopic method (at 280 and 260 nm). Succinylation of the phage samples was conducted according to the method developed by T.J. Molenaar. The phage's lytic activity spectrum was determined through spot tests on 224 strains of the *Pseudomonas* genus and 106 strains of other genera (correspondingly, of strains *Enterobacter* -40, *Escherichia* -10, *Citrobacter* -8, *Hafnia* -7, *Serratia* -6, *Shigella* -10, *Salmonella* -8, *Proteus* -7) through the use of a phage suspension containing $10^5 - 10^6$ PFU/ml. (This concentration of infectious phage corpuscles corresponds with the critical distribution of the M6 phage). The results of the research were subjected to statistical processing using single-factor dispersion analysis. **Results and discussion.** One hundred percent phage protein acylation leads to a loss of adsorption ability on sensitive cells and is accompanied by a significant (more than 10^3 times) decrease in the level of specific lytic activity in the phage preparations. The succinylation type being studied does not cause changes to the morphology or antigen structure of phage virions and does not substantially affect the lytic activity spectrum or the average yield of infectious phage corpuscles on a single sensitive bacterial cell. Considering the relative uniqueness of any biological object (including the M6 phage being studied), the authors recognize the advisability of verifying the established patterns of the effect of various acylation levels on the biological properties of other types and morphological groups of viruses. It was proven that at phage sample acylation levels of 5%, 10%, and 20%, the specific lytic activity increased by a factor of ninety, twelve, and eight respectively. The adsorption speed constant increased by a factor of nine, eight, and eight respectively. And the duration of the latent period fell by 20% in all cases with the development of a productive infection caused by the acylated samples of the phages. The use of this chemical modification method does not cause changes to the morphology or antigen structure of phage virions and does not substantially affect the average yield of infectious phage corpuscles on a sensitive bacterial cell.

Key words: acylation, adsorption speed, lytic activity, *Pseudomonas* M6 bacteriophage.

ОПРЕДЕЛЕНИЕ СПЕКТРА ГЕНОВ РЕЗИСТЕНТНОСТИ К АНТИБИОТИКАМ У ФЕНОТИПИЧЕСКИ РЕЗИСТЕНТНЫХ ШТАММОВ ПРИСТЕНОЧНОЙ КИШЕЧНОЙ МИКРОБИОТЫ У КРЫС МЕТОДОМ ПЦР-РВ Букина Ю.В., Камышный А.М., Полищук Н.Н.

21-27

DETERMINATION OF THE SPECTRUM OF ANTIBIOTIC RESISTANCE GENES HAVE PHENOTYPIC RESISTANT STRAINS OF PARIETAL INTESTINAL MICROBIOTA IN RATS BY RT-PCR

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Introduction. The problem of formation of bacterial resistance to glycopeptides and beta-lactam antibiotics (cephalosporins and carbapenems) are used worldwide for the treatment of severe community acquired and nosocomial infections, especially caused by polymicrobial flora has become global and is a major factor limiting the effectiveness of antibiotic therapy. In this regard, the study of genetic microbial resistance determinants allows not only to carry out an effective antibiotic therapy, but also to identify two main processes leading to the development of epidemiologically significant events: the introduction of the agent in the risk population from the outside and in situ pathogen (spontaneous genetic drift) targeted restructuring of the population. Therefore, the aim of our study was to investigate the resistance genes to carbapenems, cephalosporins, glycopeptides have clinically important phenotype of resistant strains of microorganisms families Enterobacteriaceae, Pseudomonadaceae, Bacteroidaceae, Enterococcaceae, Peptostreptococcaceae.

Materials and methods. As a material for PCR studies 712 phenotypically resistant strains of microorganisms isolated from 80 rats "Wistar" line in microbiological study microflora of the wall were used. During the investigation 474 isolates of bacteria of the family Enterobacteriaceae, 39 - Pseudomonadaceae, 71 - Bacteroidaceae, 96 - Enterococcaceae, 32 - Peptostreptococcaceae were studied. Isolation of DNA from bacteria in the study was performed using reagents "DNA-Express" ("Litekh", Russia). For the detection of resistance genes by PCR in real time (RT-PCR) reagent kits "FLUOROPOL-RV" ("Litekh", Russia) were used. During the experiment, the VIM genes, OXA-48, NDM, KPC, responsible for the resistance of microorganisms to carbapenems, CTX-M - resistance to cephalosporins, as well as genes Van A and van B, the development of resistance to glycopeptides (vancomycin and teicoplanin) were determined. Analysis of the results of amplification was performed using the program Bio-Rad CFX Manager 3.0 under the "Guidelines on the application of Fluoropol format sets - PB." **Results and discussion.** During the study of 474 cultures of microorganisms - representatives of the Enterobacteriaceae family, KPC - in 7,81% and OXA-48 - in 8,44%, VIM detected in 14,14% of the strains, NDM - 8,23% in the studied crops. These genes were detected in *E.coli* strains (6,74%, 7,87%, 14,61%, 4,49%, respectively), from microorganisms of the genus *Klebsiella* (13,85%, 1,54%, 15,38%, 12,31%), *Salmonella* (7,03%, 10,16%, 13,28%, 8,59%), *Enterobacter* (4,76%, 14,29%, 15,87%, 4,76%), *Proteus* (7,89%, 10,53%, 14,47%, 6,58%) and *Shigella* (7,55%, 3,77%, 11,32%, 15,09%). In the study of *Bacteroides* (*Bacteroides* spp.) Genes KPC, OXA-48, the VIM and NDM were identified in 9,86%, 4,23%, 9,86% and 12,68% of the strains, respectively. PCR study of 39 isolates of *P.aeruginosae* showed the presence of only VIM gene and only 15,38% of the cultures. In the family Enterococcaceae and Peptostreptococcaceae these genes were not found. According to Russian researchers have identified strains of Enterobacteriaceae only genes OXA-48 (43,7%) and VIM (17,6%), and VIM gene detection rate in *P.aeruginosae* was 62.9%. CTX-M gene was detected in 10,97% of the strains of the family Enterobacteriaceae (*Klebsiella* spp. - 13,85%, *Salmonella* spp. - 14,6%, *Enterobacter* spp. - 7,93%, *Proteus* spp. - 6,58%, *Shigella* spp. - 13,21%), Bacteroidaceae - 15,49%, Peptostreptococcaceae - 6,25%. In *Pseudomonas* and *Enterococcus* CTX-M is not revealed. At the same time, according to the literature, the frequency of detection of gene CTX-M in the family Enterobacteriaceae strains circulating in the Russian Federation, in some regions reaches 100%, thus, the gene is not detected in enterococci and *Pseudomonas*. In Enterococcaceae phenotypically resistant strains of microorganisms of the family genes in identifying Van A and Van B 11,46% and 6,25% causing resistance to glycopeptides, particularly vancomycin. Thus, of the 46 strains studied *E.faecalis*, 10,87% of isolates possessed Van A genes and 8,7% - Van B. Out of 50 studied cultures *E.faecium* 12% were in their genotype Van A and 4% - Van B. However, the frequency of detection of genes Van A and Van B in *E.faecalis* strains circulating in Russia, 1,7% and 2,2%, while *E.faecium* - 9,3% and 11,5% respectively. Bacteria of the family Peptostreptococcaceae these genes were not identified. During the molecular genetic studies we have not detected phenotypically resistant strains that have combined carbapenemases activity. **Conclusions.** The findings of the research results indicate the presence of carbapenem resistance genes in strains of microorganisms families Enterobacteriaceae, Bacteroidaceae and Pseudomonadaceae (*P.aeruginosae*), to cephalosporins - Enterobacteriaceae, Bacteroidaceae and Peptostreptococcaceae, vancomycin - from family Enterococcaceae bacteria. Phenotypically resistant strains that have combined carbapenemases activity, not revealed. Despite the wide range of activity of appointment carbapenems, cephalosporins and vancomycin should take into account the results of determination of resistance genes causing resistance to these drugs. It is advisable to creating circulation monitoring program of antibiotic-resistant strains, including those with carbapenemases activity in humans and in the environment.

Keywords: antibiotic resistance, gene indication, resistance genes, RT-PCR, parietal microflora.

ЭФФЕКТИВНОСТЬ *VACILLUS COAGULANS* В ЛЕЧЕНИИ АНТИБИОТИК-АССОЦИИРОВАННОЙ ДИАРЕИ НА ФОНЕ ИНДУЦИРОВАННОГО ИММУНОДЕФИЦИТА У МЫШЕЙ

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Носальская Т.Н., Мартынов А. В., Бомко Т.В., Каблучко Т.В.

BACILLUS COAGULANS EFFICIENCY IN TREATING ANTIBIOTIC-ASSOCIATED DIARRHEA IN IMMUNODEFICIENCY MICE

Nosalskaya T.N., Martynov A.V., Bomko T.V., Kabluchko T.V.

Introduction. One of the most promising probiotic including spore-forming microorganisms is a lactobacilli *Bacillus coagulans* (BC). In the spore form, it is resistant to technological processes and storage, it does not collapse under the influence of gastric juice and bile. After getting into the duodenum, the BC spores can germinate into vegetative bacteria in the human intestine and exert their probiotic effects. BC is not a part of dietary supplements. Recently, many drugs with proven clinical efficiency, based on BC, in the global pharmaceutical market are present. Based on the BC, the drug Laktovit Forte's influence on the digestive disorders and intestinal dysbiosis caused by streptomycin chronic administration in immunodeficiency mice was investigated in this study. **Materials and methods.** Work carried out on white outbred mice weighing 20-22 g to simulate digestion disorders characterized by diarrhea in mice for 9 days through streptomycin administered intragastrically at a dose of 2 g / kg of body weight. Disorders in the immune status were modeled by a single subcutaneous injection of cyclophosphamide at a dose of 250 mcg / kg. A *Bacillus coagulans* from Laktovit Forte was administered to the animals of experimental groups intragastrically at a dose of 46 mg / kg. Comparison drugs were capsules containing Lactobacillus acidophilus (LA-5) and Bifidobacterium animalis subsp. lactis (BB-12). Comparison drugs were also administered intragastrically at a dose of 42 mg / kg. Both drugs were administered beginning from day 6 after antibiotic was started to be administered, the treatment duration was for 7 days. Animals were randomized into groups by 12 animals each: 1 - intact control; 2 - control disease (only streptomycin administered); 3 - pathology with immunosuppression (both streptomycin and cyclophosphamide administered); 4 - streptomycin + Laktovit Forte; 5 - pathology immunosuppression + Laktovit Forte; 6 - streptomycin + reference drug; 5 - pathology immunosuppression + reference drug. **Results and discussion.** Laktovit Forte (BC) showed pronounced Antidiarrheal effect - the effect was 75%, and in immunodeficiency conditions only 50%. The antidiarrheal effect of the drug based on comparison lactobacilli was 60% in both groups. Similar trends were observed in level of intestinal motility. The Laktovit Forte decreased high intestinal motility during pathology at 61%; in immunosuppression conditions - only 54%. Comparing the drug produced a less pronounced effect, but similar in the groups with and without immunosuppression - respectively 44.5 and 45.9%. BC effects differently under immunosuppressant conditions and without; indicating the importance of immune component in the mechanism of its action in antibiotic-associated diarrhea. The drugs based on comparison bacteria have less pronounced effect, indicating that its probiotic effects and the absence of immune system direct stimulation. The Laktovit Forte is also more effective in preventing body weight loss in animal than comparison drug on the background of the development pathology. For all studies indicates Laktovit Forte was significantly more effective than the drug on the other lactobacillus. **Conclusion.** *Bacillus coagulans* from Laktovit Forte provided antidiarrheal effect not only due to the antagonistic probiotic action, but also due to direct stimulation of the immune system.

МІКРОЕКОЛОГІЯ СЛИЗОВОЇ ОБОЛОНКИ АЛЬВЕОЛЯРНИХ ГРЕБНІВ В ПЕРІОД АДАПТАЦІЇ ДО ПОВНИХ ЗНІМНИХ ПРОТЕЗІВ

Янішен І.В., Сохань М.В., Осолодченко Т.П., Пономаренко С.В., Межибецький Д.О.

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MICROECOLOGY OF THE MUCOUS MEMBRANE OF THE ALVEOLAR RIDGES IN THE PERIOD OF ADAPTATION TO COMPLETE DENTURES

Yanishen I. V., Sokhan M. V., Osolodchenko T. P., Ponomarenko S. V., Mezhybetskyi D. O.

Introduction. The oral cavity is an open ecosystem for various microorganisms and is one of the most populated biotopes of human. Removable dental prosthesis creates favorable conditions for the breeding of various microorganisms, including fungi. Stomatitis of dentition (SOD) refers to a group of the most frequent pathologies of the mucous membranes of the oral cavity inflammatory character, due to the presence of the patient's dental prosthesis. For the prevention of SOD due to removable prostheses are used proper hygiene of dental prostheses, manufacture of technologically optimal designs of dentures, the shielding of the prosthesis and the use of cushioning materials. In this regard, the aim of this work was to study the dynamics characteristics of the microbiota of the mucous membranes of the oral cavity when performing prosthetic rehabilitation of patients with complete removable acrylic dentures with the use of adhesive and without its use. **Materials and methods.** The formation of the clinical groups of the patients occurred according to the following criteria: the study group comprised 23 patients with complete edentulous upper and lower jaw, which produced full removable laminar dentures on the upper and lower jaw, which used water-resistant adhesive based on polyvinylacetate and carboxymethylcellulose (cushions and/or cream "Fittydent") according to the instructions of the manufacturer, the control group consisted of 12 patients with complete edentulous upper and lower jaw, which produced full removable laminar dentures on the upper and lower jaw, in the period of adaptation to removable dentures has not applied the adhesive to improve the fixation of dentures. Microbiological examination of patients was carried out in dynamics before developing the prosthesis, after a week and after a month's stay of the prosthesis in the oral cavity. **Results and discussion.** Microbiological studies included determination of the qualitative and quantitative composition of the biocenosis. It is established that the microflora of the alveolar ridge in patients with edentulous consisted of associations of yeasts from 2-5 representatives of the microbial world. It is established that in patients of the experimental group on the 7th day of withdrawal 3-component microbial associations has decreased in 1.3 times, whereas the 4-component associations were recorded in 1.4 times more often compared with the initial period of observation. For patients with adhesive frequency of detection of 2-component microbial associations 30-the day of the research was 1.3 times higher than prior to the setting of the prosthesis. Identify 5 component associations for 30-the day, has decreased in 2 times. In patients without adhesive (control group) 4-component microbial associations in the mouth after a week of adaptation to the prosthesis were detected in 1.6 times, and 30 days – in 2 times more often than to prosthetics. The weight 5 component associations through the week remained at the initial level, while after 30 days has increased in 1,5 times. The structure microbiocenosis the mucous of the oral cavity patients with edentulism are represented 13 genera of bacteria and morilloid fungi of the genus *Candida*, allocated in secondary amounts by lg (2,5±0,19) to lg (5,4±0,17) CFU/g. When adhesive between denture base and mucosa of the alveolar ridge frequency of withdrawal and the density of microbial colonization in the adaptation period were not statistically different. But the density of the microbial population among the control group increased 1.5 times for *Enterococcus spp*, 1.4 for the *Klebsiella spp* and 1.6 times for yeast fungi *Candida spp*. Found a significant decrease in microbial density of the representatives of the resident microflora in 1.4 times for *Neisseria spp*, 1.6-fold for *Lactobacillus spp* (p<0.05). **Conclusion.** The results of these studies indicate significant changes of qualitative and quantitative structure of microbiocenosis of oral cavity in patients with edentulous representatives *Moraxella spp*, *Klebsiella spp* and *E. coli* Comparison of frequency of discharge and the density of microbial colonization showed persistence in a given habitat representatives of 13 genera of bacteria and yeast fungi of the genus *Candida* in medium quantities from lg (2,5±0,19) lg to (5,4±0,17) CFU/g. For patients who used adhesive (fixative cream and/or cushions Fittydent) on the basis of carboxymethylcellulose and polivinilatsetat in the period of adaptation to removable prosthesis characteristic was reduced in 2 times revealing the 5 component associations on 30 the day. Frequency of withdrawal and the density of microbial colonization of the experimental group were not statistically different. Among patients in the control group increased the density of microbial colonization for *Enterococcus spp*, *Klebsiella spp* and yeasts of *Candida spp*. Found a significant decrease in microbial density of the

representatives of the resident microflora in 1.4 times for *Neisseria spp*, 1.6-fold for *Lactobacillus spp*. Identified microbiological characteristics dictate the need for inclusion in the treatment of patients with edentulous circuit correction of microbiocenosis of the oral cavity, with the use of the funds are directed anti-inflammatory action and ensure the restoration and preservation of normal biocenosis of the specified biotope.

Key words: microecology, adaptation, adhesive, complete dentures.

ВИВЧЕННЯ ПРОТИМІКРОБНОЇ АКТИВНОСТІ КОМБІНАЦІЙ ФОСФОМЦИНУ З ЦЕФЕПІМОМ ТА ФОСФОМЦИНУ З ТІСНАМОМ ЩОДО ПОЛІАНТИБІОТИКОРЕЗИСТЕНТНИХ ШТАМІВ ЕНТЕРОБАКТЕРІЙ
Дяченко В.Ф., Марющенко А.М., Чигиринська Н.А., Куцай Н.М.

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THE STUDY OF ANTIMICROBIAL ACTIVITY OF COMBINATIONS OF FOSFOMYCIN WITH CEFEPIME AND FOSFOMYCIN WITH TIENAM IN RESPECT POLYANTIBIOTIC-RESISTANT STRAINS OF ENTEROBACTERIA
Dyachenko V.F. Mariushchenko A.M., Chygyrynska N.A., Kutsay N.

Introduction. The rapid decrease in sensitivity of pathogens of septic infections to antimicrobial agents has led to significant difficulties in the treatment of antibiotic-resistant infections. One solution of this problem is the method of combining of antimicrobial medications from different pharmacological groups. Antimicrobial synergy resulting from antibiotic combination therapy is often important in the treatment of serious bacterial infections. The aim of the study is investigation of combined antimicrobial action of fosfomycin with cefepim and fosfomycin with tienam in respect polyantibiotic-resistant strains of enterobacteria. **Materials and methods.** The polyantibiotic-resistant strains used in this study were isolated from patients hospitalised in the Hospital of Kharkov. The study of combinations of antibiotics efficacy was carried out by determining the minimum inhibitory concentrations using routine in vitro "checkerboard" method. **Results and discussion.** Calculation of the fraction inhibitory index showed that the combination of fosfomycin with cefepime demonstrated synergistic inhibitory activity against 71,43 % of enterobacteria strains tested; combination of fosfomycin with tienam result in summation or indifferent effect against 71,43 % polyantibiotic-resistant strains of enterobacteria. **Conclusion.** Thereby combination of fosfomycin with cefepime may be considered as synergistic and perspective for further experimental in vivo studies and studies of their clinical effectiveness against polyantibiotic-resistant strains of enterobacteria – causative agents of pyoinflammatory diseases.

Key words: combinations of the antibiotics, polyantibiotic-resistant strains, "checkerboard" method.

ЕКСПЕРИМЕНТАЛЬНІ РОБОТИ, ФАРМАЦІЯ
Experimental papers, pharmacy

COMPARATIVE STUDY OF ANTIBACTERIAL ACTIVITY OF PEROXYDISUCCINIC ACID, HYDROGEN PEROXIDE AND THEIR MIXTURE
Blazheyvskiy M. Ye., Boyko N. N., Prysiazhniuk O. V.

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Introduction. It is known that reactive oxygen species (ROS) generated in vivo by cell aerobic metabolism cause multiple damage in different cell organelles and kill not only obligate anaerobes and microaerophiles, but also aerobes. ROS generated by phagocytes and representatives of normal microflora are an important component of macroorganism defense from most pathogens, which is explained by their ability to damage different biological structures. ROS have high reactivity and let us use them in vitro as effective biocides. Hydrogen peroxide is widely used in many industries, in particular, in medicine and veterinary as antiseptic and disinfectant agent due to its safety for environment and broad spectrum of antimicrobial activity including spore-forming bacteria. However, in the recent years certain decrease of background sensitivity of microorganisms to hydrogen peroxide and occurrence of resistant strains of pathogenic microorganisms to this agent has been noted. The aim of this work is to carry out a comparative study of antimicrobial activity of hydrogen peroxide, peroxydisuccinic acid (PDSA), monoperoxydisuccinic acid (MPSA), and mixture of PDSA and hydrogen peroxide (H₂O₂). **Materials and methods.** The substances of peroxydisuccinic acid (PDSA) and monoperoxydisuccinic acid (MPSA) were prepared by well known methods. The following test-strains were used to assess antimicrobial activity of the agents: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Pseudomonas aeruginosa* ATCC 9027, *Basillus cereus* ATCC 10702, *Basillus cereus* ATCC 96, *Basillus subtilis* ATCC 6633, *Proteus vulgaris* ATCC 4636, *Candida albicans* ATCC 885/653, and *Candida albicans* ATCC 10231. All disinfectant agents were diluted in distilled water at 40 °C and stirred. The microbial burden was 2·10⁹ CFU/ml of the medium, and for kinetic studies 10⁵ CFU/ml of the medium, it was standardizing according to McFarland standard. Microorganisms' resistance to disinfectant agents was determined by seeding of the diluted cell suspension on agar medium after their incubation with MPSA, PDSA, H₂O₂, and also after MPSA generation in the reaction between PDSA and H₂O₂, and seeding of the cell suspension with exclusion of these factors was taken as control. 18-24-hour microorganism culture was taken into work. Mueller-Hinton agar and MPA were used for bacteria. Sabouraud agar was used for *Candida albicans*. Agar well diffusion method was applied. Determination of antimicrobial activity of the agents were carried out on two layers of solid medium in Petri dishes. In kinetic study of microorganism's death rate due to incubation period with peroxide solution tested, the bactericidal action was stopped with 5 % sodium thiosulfate sterile solution. All studies were carried out in 3 replicates. In statistical analysis methods, significance level P was equal to 0.95. Student's test was used for statistical processing of the data obtained. **Results and discussion.** It has been found that treatment of *S. aureus* ATCC 25923, *E. coli* ATCC 25922 test-strains for 60 min with 3% (and even 6% H₂O₂ for *E. coli*) does not cause total death of microorganisms. The fact of resistance of spore-forming cultures *B. cereus*, *P. aeruginosa* and *C. albicans* to hydrogen peroxide should be noted, in 60 min of their incubation with 6% H₂O₂, the number of viable cells decreased from 5.0 to 1.58 lg CFU/ml, as well as to 3.00 (to 1.84 for 120-min exposition) and 1.65 lg CFU/ml, respectively. However, pretreatment of test-stains by 5-fold diluted mixture of 3% H₂O₂ and 1% PDSA for 60 min caused total death of *S. aureus* and *E. coli*, and decreased the number of viable cells of *B. cereus* spore-forming cells and relatively resistant to hydrogen peroxide cultures of *P. aeruginosa* и *C. albicans* from 5.00 to 1.34 and 0.95 lg CFU/ml, respectively, and in 120 min to their total death. **Conclusions.** The study have determined that antimicrobial effect of reactive oxygen species (ROS) produced by interaction of hydrogen peroxide and peroxydisuccinic acid (PDSA) mixture in the synergistic system is many times higher and faster achievable than hydrogen peroxide or peroxydisuccinic acid only. We have determined the principles of optimum conditions for ROS generation by choice of respective concentrations of peroxydisuccinic acid and hydrogen peroxide. ROS demonstrate high biocidal activity and short lifetime, which allows us to consider the combination of hydrogen peroxide and peroxydisuccinic acid as a promising means for development of a highly efficient disinfectant with a broad spectrum of antimicrobial activity and without a tendency to accumulate in the environment.

Key words: reactive oxygen species (ROS), bacteria, biocide, disinfectant, hydrogen peroxide, peroxydisuccinic acid, synergetic composition.

DEVELOPMENT OF METHOD OF QUALITATIVE ANALYSIS OF BIRD CHERRY FRUIT FOR INCLUSION IN THE MONOGRAPH OF STATE PHARMACOPOEIA OF UKRAINE

50-53

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Introduction. Bird cherry *Padus avium* Mill, *Rosaceae*, is widespread in Ukraine, especially in forests and forest-steppe areas. Bird cherry fruits have long been used in medicine and is a valuable medicinal raw materials. They stated to possess astringent, anti-inflammatory, phytoncidal properties. Bird cherry fruits are included in the USSR Pharmacopoeia IX ed., The State Pharmacopoeia of the Russian Federation, The State Pharmacopoeia of Republic of Belarus. In Ukraine there are no contemporary normative documents for this medicinal plant material, therefore it is the actual to develop projects in the national monographs "dry bird cherry fruit" and "fresh bird cherry fruit" to be included in the State Pharmacopoeia of Ukraine. According to European Pharmacopoeia recommendation method of thin-layer chromatography (TLC) is prescribed only for the identification of the herbal drug. The principles of thin-layer chromatography and application of the technique in pharmaceutical analysis are described in State Pharmacopoeia of Ukraine. As it is effective and easy to perform, and the equipment required is inexpensive, the technique is frequently used for evaluating medicinal plant materials and their preparations. The TLC is aimed at elucidating the chromatogram of the drug with respect to selected reference compounds that are described for inclusion as reagents. Aim of this study was to develop methods of qualitative analysis of bird cherry fruits for a monograph in the State Pharmacopoeia of Ukraine (SPU). **Materials and Methods.** The object of our study was dried bird cherry fruits (7 samples) and fresh bird cherry fruits (7 samples) harvested in 2013-2015 in Kharkiv, Poltava, Luhansk, Sumy, Lviv, Mykolaiv regions and the city Mariupol. Samples were registered in the department of SPU State Enterprise "Pharmacopoeia center". In accordance with the Ph. Eur. and SPU requirements in "identification C" determination was performed by TLC. TLC was performed on glass-backed silica gel F₂₅₄ Merck plates, size 20x10 cm. Test solutions from samples of dried raw material were prepared by extraction of 1% solution of hydrochloric acid in 95% ethanol with ultrasound for 60 minutes at 50° C. As mobile phase solvent mixture ethyl acetate - anhydrous acetic acid - formic acid - water ratio (100: 10: 10: 25) was selected. For preparation the reference solution 1 mg chrysanthemin was dissolved in 10 mL of 1% solution of hydrochloric acid in 95% ethanol. Fresh bird cherry fruits test solutions of the samples were crushed to mash (free of seeds), 10 mL of methanol was added and treated with ultrasound for 15 minutes. As mobile phase solvent mixture formic acid anhydrous-water-butanol ratio (16:19:65) was selected. Two reference solutions were used. First was prepared from 2 mg chrysanthemin dissolved in 5 mL of methanol and second was Pharmacopoeial Reference Standard SPU of bird cherry extract dissolved in 0.2 mL of methanol with ultrasound bath. Test solutions and the reference solutions were placed onto the chromatographic plates and placed into the chamber. When the chromatograms developed, the plates were taken out, then observed the spots in daylight. **Results and discussion.** In the chromatogram it was observed for all dry bird cherry fruits samples two pink-red color zones, one of which coincided for R_f and color of chrysanthemin, and the other one was slightly lower. The chromatogram for all samples of fresh raw material showed two pinkish-violet zones, one of which had R_f and color corresponded chrysanthemin, and the second one was slightly lower. Compared with bird cherry extract, it was observed two pinkish-violet zones, coincided with R_f and color of bird cherry (SPU) extract zones. In accordance with the requirements of Ph. Eur. identification by TLC is obligatory. Division of anthocyanins of plant raw materials was observed sufficiently in our chosen solvent systems and methods of analysis that allows to recommend these systems and methods of analysis for inclusion in the relevant sections of monographs for bird cherry fruit, dried and fresh for SPU. **Conclusion.** It was confirmed the opportunity to include in the national monographs "Bird cherry fruits fresh" and "Bird cherry fruits dry" in section "Identification C" analysis of anthocyanin by TLC in chosen systems and methods.

Key words: bird cherry, TLC, State Pharmacopoeia of Ukraine

ВОЗМОЖНОСТЬ ПРИМЕНЕНИЯ СЖИЖЕННЫХ ГАЗОВ ДЛЯ ОЧИСТКИ АЛКАЛОИДОВ БАРБАРИСА

54-58

Демьяненко Д. В., Демьяненко В. Г.

POSSIBILITY FOR APPLICATION OF LIQUEFIED GASES FOR PURIFICATION OF BARBERRY ALKALOIDS

Demyanenko D. V., Demyanenko V. G.

Introduction. Biologically active substances (BAS) of barberry roots represented by alkaloids of isoquinoline group are perspective substances for development of preparations with multiple pharmacological activities. However, now manufacture of them in Ukraine is stopped. One of the reasons of this is out-of-date production technologies of alkaloids involving use of toxic and/or flammable solvents. In the article possibility for application of liquefied gases in technology of obtaining of alkaloids from barberry roots has been studied. **Materials and methods.** Initial raw herb drug were barberry (*Berberis vulgaris*) roots harvested in spring on the territory of Southern Ukraine. Their moisture content was 11%, comminuting degree was 0,5-1,4 mm. At the first stage purification of raw herb drug from lipophilic impurities (defatting) was made with use of some liquefied gases: tetrafluoroethane, isobutane, difluorochloromethane and difluoromethane. Extraction of the alkaloid sum was made with difluoromethane mixed with various quantities of liquid ammonia or diethylamine as alkaline agent. Crude extracts were exposed to two-level liquefied-gas purification. At first the alkaloid bases were transformed into saline forms with aqueous solutions of acids and purified from ballast impurities with liquefied freon-22. Then alkaloid salts were reextracted from aqueous phase in the base form with liquefied mixture of difluoromethane and ammonia. Mixing of liquid phases was provided by creation of alternate gradients of temperatures and, as consequence, pressures between separators feeding alternately cool water into jacket of one of them, and warm water – into jacket of another one. Quantity of lipophilic ballast impurities and also weight of extractives were determined gravimetrically. Quantitative analysis of the alkaloid sum was made by titrimetric method after sedimentation of alkaloids with volumetric solution of phosphomolybdic acid. **Results and discussion.** It has been found that at stage of degreasing of raw crude drug the most selective solvent to lipophilic ballast compounds was isobutane and difluorochloromethane, but the latter was more rational for using in industrial scale concerning its fire-safety and economic availability. It has been also found that efficiency of the purification stage of Berberis alkaloids appreciably depends on composition of extracting solvent while obtaining of crude extracts. The best parameters in the finished product have been revealed after purification of the extracts obtained with difluoromethane containing 12% of liquid ammonia: quantity of BAS (alkaloids) in the finished product reached 95%, and their losses were insignificant – 3,5%. Increasing of cosolvent (ammonia) content in the extracting solvent considerably complicated purification of extractives, and losses of alkaloids raised to 13,2%, obviously as a result of presence of considerable quantity of hydrophylic ballast substances. Reducing of the ammonia content in the extracting solvent down to 1% also caused negative impact on process of obtaining of the alkaloids which yield was the lowest among investigated assays. It's possible to explain this by lower pH value in extracting medium, change of solvent polarity, therefore middle-polar and hydrophobic compounds preferably passed into composition of crude extracts. **Conclusions.** Acceptability for use of liquefied gases and their mixtures for purification of the alkaloid sum from barberry roots has been proved. It has been shown that prior to stage of extraction of these BAS it's expedient to withdraw lipophilic impurities from the crude herbal drug with liquified difluorochloromethane (freon-22). Purification efficiency of the finished product considerably depends on composition of extracting solvent during obtaining of crude extracts. The best parameters were

found after purification of the extracts taken with difluoromethane containing 12% of liquid ammonia. It's the most expedient to purify crude extracts by two-step procedure using on the first step liquefied difluorochloromethane (freon-22) as organic phase and on the second one – difluoromethane mixed with 10% of ammonia, and as aqueous phase – 10 % acidic solutions; at the second step it's necessary to provide liquid re-extraction of the alkaloid bases in triplicate.

Keywords: barberry roots, alkaloids, liquefied gases, purification.

ДОСЛІДЖЕННЯ МІКРОХВИЛЬОВОЇ СУШКИ ГРАНУЛ ЦЕОЛІТУ ПРИРОДНОГО ТА ЇЇ ВПЛИВУ НА ТЕХНОЛОГІЧНІ ВЛАСТИВОСТІ

59-64

Рибачук В.Д.

RESEARCH OF MICROWAVE DRYING OF NATURAL ZEOLITE GRANULES AND ITS INFLUENCE ON THE TECHNOLOGICAL PROPERTIES

Рибачук В.Д.

Introduction. The wet granulation technique is often used in the preparation of free-flowing granules in the manufacture of tablets and capsules. It is very important that granules obtained by this technology be dried before further processing. And also, it is important that the method of drying is entirely controlled and managed and the result is quite predictable. In recent years, microwave drying of granules make a considerable interest. Microwave drying is especially useful for moisture sensitive materials which are mostly pharmaceutical substances. Microwave drying technology is useful for dosage forms with high purity, since this method provides the possibility of drying in the same container production, which reduces the chance of cross contamination of matter and its direct contact with staff. The aim of this work was to study the effect of microwave radiation on the technological properties of natural zeolite peets compared to traditional convection method and to determine the optimal drying modes and specific humidity of the material. **Material & methods.** Granules were prepared by wet granulation technology by using a laboratory granulator NG-12. As the humidifier we used potato starch gel and PVP in an amount of 25% by weight of the dry product. The resulting granules were divided into two equal parts and subjected to drying in a microwave oven (Delfa D20MW) of installed capacity (119 W, 280 W, 336 W, 462 W, 595 W and 700 W) and shelf dryer to a residual moisture level of 0.01 g.w./g.d.m. or less. Determination of the specific humidity of granules was carried out by mass loss on drying. Fractional composition of granules was determined using a standard set of sieves with the diameter of the holes 2.0; 1.0; 0.5 and 0.25 mm. The friability of the granules was determined using friabilator Pharma Test PTF 10E / ER, Germany. To characterize the fluidity of granule Carr's indicator (I_c) and coefficient Hausnera (H_R). **Results & discussion.** The results of experimental studies have shown a significant impact of intensity microwave radiation on the rate of drying material. With an increase in power from 119 watts to 700 watts time spent on drying decreased more than twice. Changing the speed of drying material took place in two periods. In the first period (humidity of 0,29-0,05 g.w./g.d.m.) free moisture located mainly on the surface of the granules is removed in the first period, in the second period (0,04-0,05 g.w./g.d.m.) moisture from the inner pores of the material is removed. Type of drying does not significantly affect the distribution of particle size. Different amounts of microwave radiation also not significantly affect the size and rheological properties of the granules. The last one was confirmed by values of Carr's index and coefficient of Hausner. Both indicators showed that all series of obtained granules have very good flowability. Study of the influence of specific humidity values on the mechanical strength of granules and tablets obtained on the basis showed that its most optimal level, which can be recommended both for granules and for tablets, is based on their range of 0,03-0,05 g.w./g.d.m. Knowing the limits of specific humidity allows to choose optimal modes of power microwave radiation for drying a natural zeolite granules. **Conclusion.** The effect of microwave radiation on the dynamics of natural zeolite pellets drying on the value of their technological properties. Optimal levels of specific humidity for granules and tablets, providing the best technological properties, is 0,03-0,05 g.w./g.d.m. On the basis of data obtained, the reasonable duration of the process of drying, depending on the power of the microwave radiation, is 3-14 minutes.

Keywords: natural zeolite, granules, microwave drying, humidity, technological properties

РОЗРОБКА СКЛАДУ ВІТЧИЗНЯНОГО ІНФУЗІЙНОГО ПРЕПАРАТУ НА ОСНОВІ ПАРАЦЕТАМОЛУ

65-68

Алмакаєва Л.Г., Науменок Л.Г., Бегунова Н.В., Доля В.Г., Алмакаєв М.С.

DEVELOPMENT OF DOMESTIC INFUSION DRUGS BASED ON PARACETAMOL

Алмакаєва Л.Г., Науменок Л.Г., Бегунова Н.В., Доля В.Г., Алмакаєв М.С.

The intravenous form of paracetamol compared with oral more reliably supports effective drug concentration in blood plasma that promotes a higher therapeutic effect. Recent studies have confirmed that the use of the intravenous form of paracetamol to deal with postoperative pain multimodal analgesia modes results in reducing the frequency and quantity of opioids administered, and, as a consequence, its associated side effects. The drug Paracetamol, infusion solution 10 mg / ml to 100 ml glass bottles is a drug - generic. His qualitative and quantitative composition is developed from the study of literature data about the drug - similar to "Perfalhan, 10 mg / ml solution for infusion in 100 mL" company Bristol - Myers Squibb, France and experimental work. The aim of our study is development and support of the national composition of the infusion of the drug on the basis of paracetamol, selection of excipients that provide stability of the active substances. **Materials and methods.** The object of the study was the substance of paracetamol manufactured by Zhejiang Kangle Pharmaceutical Co., Ltd, China. During the work conducted qualitative and quantitative monitoring sample preparation for indicators of stability: pH content of the active ingredient, transparency, color, impurities, contamination by the methods described in the SFU [and non-oral documentation to the drug]. One potential factor of instability is the effect of paracetamol oxygen, due to the presence in the molecule of paracetamol and -NH possibility of oxidation. **Results and Discussion.** Paracetamol is derived acetaminophen. Substance acetylation are p-aminophenol with acetic anhydride. Saturated aqueous solution has a pH of paracetamol - ment about 6. Paracetamol is a crystalline white powder, sparingly soluble in water, soluble in 96% alcohol, very slightly soluble in methylene chloride. Active substance enters in comparison drug in the concentration of 10 mg/ml. Stable aqueous solution decreases in acidic and alkaline environments where paracetamol gradually destroyed to acetic acid or p-aminophenol. To prevent oxidation of the drug administered antioxidant - sodium metabisulfite in concentrations generally 1.0 g / l. In order to prevent the negative impact of oxygen on paracetamol solution 10 mg / ml drug preparation was conducted under nitrogen gas protection. It is established that the use of nitrogen gas protection affects the quality of the drug. Prepared sample preparation without nitrogen gas protection did not meet project MKYA in terms of "4-aminophenol" and "color", besides a slight tendency pH change and reducing quantitative content of active ingredient. Therefore, the production of the drug "Paracetamol, infusion solution 10 mg / ml. in bottles of 100 ml" necessary solution prepared bubbling nitrogen for 20 minutes. It is established that the use of nitrogen gas protection affects the quality of the drug. the manufacture of the drug "Paracetamol, infusion solution 10 mg / ml. in bottles of 100 ml" necessary solution prepared bubbling nitrogen for 20 minutes. Calculated theoretical osmolarity of the drug - 299,47 mOsm / l. Solution osmolarity close to

osmolarity of blood, which is an important criterion when used in injection therapy. **Conclusions.** Theoretically grounded and experimentally confirmed rational composition drug infusion composition based on paracetamol. Selected auxiliaries and processing methods in the preparation of the solution, prevents oxidation of the main active ingredient, and also provide the optimum level of osmolarity solution. Results of this development are used during compile of registration dossier of preparation, analytical and technological normative documents on his production and control of quality of intermediate products and prepared products.

Keywords: infusion solution, paracetamol, osmolarity

АНТИМИКРОБНЫЕ СВОЙСТВА «ЛИПИНА» ПРИ ИНГАЛЯЦИОННОМ ИСПОЛЬЗОВАНИИ У ДЕТЕЙ, БОЛЬНЫХ БРОНХИАЛЬНОЙ АСТМОЙ

69-74

Чернуский В.Г., Попов Н.Н., Говаленкова О.Л., Летыго А.В., Кашина-Ярмак В.Л., Евдокимова Т.В.

ANTIMICROBIAL PROPERTIES «LIPIN» INHALATION USE IN CHILDREN WITH ASTHMA

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Introduction. Problems of modern pharmacotherapy of bronchial asthma (BA) in children is largely reduced to the establishment of effective dosage forms that provide the delivery of drugs in the bronchopulmonary system without affecting other organ systems. A promising area in addressing the causal treatment of asthma in children is the use of the formulation «Lipin», which is a liposome, arising by self-assembly of amphiphilic lipid complexes. **Material & methods.** The study of antimicrobial properties «Lipin» on microorganisms isolated from sputum in 135 children are hospitalized in the pulmonology department of GU «Children's Hospital road» Kharkiv about asthma in the period of exacerbation. Age was surveyed children from 5 to 14 years on average - $11 \pm 0,12$ years. The diagnosis of bronchial asthma (BA) is set according to GINA guidelines. The treatment groups were representative, randomized by age, sex, severity of the disease. Patients with asthma in all forms (atopic, non-atopic, mixed) and severity (mild, moderate, severe) received basic asthma treatment according to the Ministry of Health of Ukraine № 4.01.12-8.1178 order dated 14.12.2009, which was supplemented by liposomal formulation «Lipin» inhalation through an ultrasonic nebulizer in age dosage. All drugs used in accordance with instructions for their use, approved by the Ministry of Health of Ukraine. Microbiological examination of sputum was performed by conventional methods: for seeding solid or liquid nutrient medium, followed by isolation and isolates microscopy, biochemical and serological identification. Identification of the isolates was performed according to the position of the Ministry of Health USSR order number 535 and respectively taxonomical determination tests bacteria Burgi. The antimicrobial activity of the preparation «Lipin» was determined by the level of the minimum inhibitory concentration (MIC) - twofold serial dilution method in medium Mueller-Hilton, the minimum bactericidal concentration (MBC) - was carried out on crops of solid growth medium by the method of S. Navashin.

Statistical analysis of the results was performed using Excel applications, Statgraphics-5 with the definition average value (M) and standard error (m). The obtained data were statistically processed by parametric mathematical statistics (t-Student criterion) when $< 0,05$.

Results & discussion. While recognizing the authority of the International (GINA, 2012) and a national protocol on the principles of asthma therapy in children, it should be noted that the recommended therapy is mainly focused on the achievement of symptomatic and pathogenetic effects. In principle this is not considered part of the microbial factor not only in the induction, but also burdening the pathogenesis and clinical course of the disease in children. In this connection, studies on the effect of non-allergic (infectious) factors on the development of asthma as a multi-stage, sequential pathological process and the development of additional methods of basic therapy is relevant and allows individualized therapy protocols in relation to the etiologic factors of the disease. The study showed that in the sputum of children with asthma in all forms of the disease were determined by the following organisms: *S. pyogenes*, *S. aureus*, *E. coli*, *Pr. Mirabilis*, *Ps. aeruginosa*. In 29.6% of children with asthma from sputum were sown Association: *S. aureus* + *S. pyogenes*; *S. aureus* + *E. coli*; *S. aureus* + *Ps. aeruginosa*; *S. aureus* + *Pr. Mirabilis*. The use of corticosteroids in treatment of asthma in children contributes to the activity of biological and pathogenic properties of indigenous, transient and exogenous microflora, mainly by reducing its control alveolar macrophages. As a result, the activation of pathogenic and conditionally pathogenic microflora, leading to the development of processes in dysbiotic bronchopulmonary system and disbioy on a new bio-based implement relapse. From this it follows that even effective sanitation agents in bronchopulmonary system, the traditional routes of administration of antibacterial drugs, properly selected, taking into account the sensitivity of pathogens to them, does not prevent it from subsequent reinfection relevant pathogens located in the throat and in the bronchopulmonary system. One way to solve this problem is to use as the dosage form liposomes, which are limited microvolumes arising by self-assembly of amphiphilic lipid complexes. The basis of selection of such a drug we used in the clinic used liposomal preparation «Lipin» inhalation at dosages of age through an ultrasonic inhaler in addition to basic therapy recommended by GINA (2012) in two stages. The first stage is achieved by using «Lipin» in 135 children with asthma, aged 5 to 14 years in acute inhalation through an ultrasonic nebulizer in age dosage of 5-10 mg / kg, depending on the age of one inhalation 2 times a day for 7-10 days in children with asthma. This is the effect of biocompatibility with enzymatic and immunological systems of the body, it is anti-microbial and anti-inflammatory effect «Lipin» due to their constituent natural phospholipids - phosphatidylcholine. The second stage of antimicrobial therapy for supporting sanitizing effect is based on the ability to «Lipin» in saline to accumulate on the damaged parts of mucous bronchopulmonary tree and provide prolonged antimicrobial effect and thus prevent the proliferation of pathogenic and opportunistic microorganisms. Comparison of the spectrum of antimicrobial activity of liposomal drug «Lipin» in saline to microorganisms isolated from the sputum of an inhalation after treatment showed that antimicrobial activity «Lipin» advantageously provides bactericidal effect against pathogenic and conditionally pathogenic microorganisms. It should be noted that this formulation does not have a significant impact on the indigenous microflora of the mucous bronchial tree.

Conclusions. 1. BA in children is characterized by a complex structure combining etiologic gram-positive, gram-negative microorganisms, fungi of the genus *Candida*, and their associations, isolated from sputum and can be defined as the induction and relapse. 2. Liposomal preparation «Lipin» inhalation through the use of an ultrasonic nebulizer has a direct bactericidal effect on pathogenic and opportunistic pathogenic microorganisms isolated from the sputum of children suffering from asthma in the period of exacerbation (MIC - 2,12-3,43 mcg/ml, MBC - 3,41-12,6 mcg/ml). 3. «Lipin» pronounced bactericidal effect is in direct proportion to the dose of the drug used and the time of its effects on the microorganisms isolated from the sputum of children suffering from asthma. 4. Inhaler use liposomal drug «Lipin» at a dose of 5.10 mg / kg body weight per inhaled three times a day for 8-10 days causes bactericidal activity against Gram positive, Gram negative microorganisms and fungi of the genus *Candida*, isolated from the sputum children with asthma.

ОРГАНІЗАЦІЙНО-ПРАВОВІ ТА МЕДИКО-ФАРМАЦЕВТИЧНІ ПІДХОДИ ДО ОПТИМІЗАЦІЇ ОБІГУ ЛІКАРСЬКИХ ЗАСОБІВ ДЛЯ ЛІКУВАННЯ ГІПЕРТОНІЇ НА СЕЛІ

75-85

Шаповалова В.О., Хмелевський М.О., Шаповалов В.В.

ORGANIZATIONAL, LEGAL, MEDICAL AND PHARMACEUTICAL APPROACHES TO OPTIMIZATION OF MEDICINES' CIRCULATION FOR HYPERTONIA TREATMENT IN COUNTRYSIDE AREAS

Shapovalova V.O., Khmelevsky N.A., Shapovalov V.V.

Introduction. Parliaments of both Ukraine and the EU have ratified Association Agreement (hereinafter – Agreement), a comprehensive document which envisages bringing all areas of the law of our country in line with European Union norms. Therefore, chapter 22 of the Agreement "Public Health" gave attention as one of the most important areas of implementation. That is, the need for introduction in Ukraine of the approach, called "Health in all policy areas" provides consider of the interests of public healthcare in approving of political solutions in any area of the state activities. The organizational, medical and pharmaceutical approaches to optimization of the medicines' circulation is the improvement of the legal system of regulation of prescription and OTC medicines (drugs), determination of the circulation of drugs of different classification and legal groups, assigning drugs to one of nomenclature and legal groups (prescription or non-prescription). **Materials and methods.** Forensic and pharmaceutical researches conducted in countryside areas at the regional level on example of the Kharkiv region based on 54 communal health institutions (CHI). Materials of the research: legal framework for the organization of pharmacy of the CHI; forensic and pharmaceutical practice for the period of 2012-2015 concerning the provision with the medicines of all legal, nomenclature and classification groups for the pharmacotherapy of hypertension in the village. In conducting the research, we used the following methods: legal, documentary, comparative analysis, forensic and pharmaceutical monitoring. **Results and discussion.** According to the Statement of the Cabinet of Ministers of Ukraine from 17.08.1998 N1303 was sorted the procedure of the concessional dispensing of the drugs (for free or at 50% discount). The procedure applies to certain categories of the population and some diseases for which benefits established by applicable law. Despite the potential of this mechanism, it does not work within the budget funding. Thanks to the work of the Department on the final stage of the pilot project during the circulation of drugs and their reimbursement attracted 575 pharmacies of different ownership forms and 1253 pharmacy points, whose work is in the village carried out by medical points, general practice and family medicine. The conducted monitoring shows us that during the pilot project 72 doctors of the CHI issued more than 265.2 thousand recipes. Hypertension drugs at discount prices began to sell from pharmacies of Ukraine from 01.08.2012. Drugs released by prescription, which could only write some doctors, family doctor, cardiologist, internist and neurologist. To control this process created a single electronic register of doctors and patients. Reimbursement cost of drugs for the treatment of essential hypertension conducted from the state budget. During the implementation of these measures was made following. Order from 23.05.2012 N331 "On creation of working groups" Department organized a telephone hotline (057)705-10-64 for providing citizens, patients, most doctors, physicians, pharmacists and others with advices on the introduction and implementation of pilot projects involving scientific department of medical and pharmaceutical law, general and clinical pharmacy of the Kharkiv Medical Academy of Postgraduate Education. Order of the Department of Healthcare of Kharkiv Regional State Administration from 10.09.2014 N560 "On approval of the register of pharmacies" approved list of pharmacies and their departments participating in the pilot project, which has 576 outlets realization of drugs. **Conclusions.** Proposed the organizational, legal, medical and pharmaceutical approaches to optimization of medicines' circulation for the treatment of hypertension in countryside areas. Studied the existing legislative and regulatory framework of Ukraine on providing ofor concessional patients with hypertension drugs. Analyzed forensic and pharmaceutical risks that cause problems in access for the patients to needed medicines. Studied the example of forensic and pharmaceutical practice of imperfections in pilot project among the countryside population. Studied the system of interaction between specialists of medicine, pharmacy, state government and other industries in the area of public access to essential medicines. A review of the pilot project of reimbursement of the cost of antihypertensive medications features in the Kharkiv region, the consequences of this project for patients and healthcare of Ukraine and Kharkiv region.

Keywords: countryside area, pharmacies, circulation, medicines, drugs, hypertension, forensic pharmacy, pharmaceutical law, medical law.

ЮБІЛЕЇ, ANNIVERSARY

Професор Палій Гордій Кондратович
Славний ювілей

86-87

РЕЦЕНЗІЇ, REVIEWS

РЕЦЕНЗІЯ

на підручник для студентів вищих медичних нав-чальних закладів IV рівня акредитації
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