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INTESTINAL VIROME AND NORMAL MICROFLORA OF HUMAN: FEATURES OF INTERACTION

Bobyр V.V., Ponyatovsky V.A., Djugikowa E.M., Shyrobokov V.P.

Summary: Intestinal bacteria defend the host organism and narrow pathogenic bacterial colonization. However, the microbiome effect to enteric viruses is unexplored largely as well as role of microbiota in the pathogenesis of viral infections in general. This review focuses on precisely these issues.

In this review article, facts about viral persistence in the human gut are summarized. It is described the role of viral populations during health and diseases. After analyzing of the literary facts it was concluded that the gastrointestinal tract is an environment for one from the most complex microbial ecosystems, which requires of more deeper study of its composition, role in physiological processes, as well as the dynamics of changes under influence of the environment. Normal microflora performs a different important functions providing the physiological homeostasis of the human body, including, in particular, an important role in the human metabolic processes, supporting of homeostasis, limiting of colonization by infectious bacteria. The multifactorial significance of the normal gastrointestinal microflora can be divided into immunological, structural and metabolic functions. At the same time, interaction between intestinal microflora and enteric viruses has not been studied largely. In recent years, much attention is paid to study of viruses-bacteria associations, and it is possible, obtained results should change our understanding of microbiota role in the systematic pathogenesis of the diseases with viral etiology. In contrast to the well-known benefits of normal microflora to the host, the viruses can use intestinal microflora as a trigger for replication at the optimal region. Recent studies give a reason for assumption that depletion of normal microflora with antibiotics can determining the antiviral effect. Thus, the role of commensal bacteria in viral transmission and pathogenesis is clarified. Probably, bacterial microflora can implement the protective role as well as be abettor of virus. However, an understanding of interaction between microbiota and virus during viral disease may initiate the introduction of new antiviral strategies. Further research is needed to determining the features of relationship between viruses and bacteria in the development of infectious process, and analyze whether the viral and bacterial agents form a symbiotic relationship in human body. This review focuses on precisely these issues.

Keywords: microbiome, virome, normal microflora, enteric viruses, contagiousness.

ИНТЕГРАЛЬНАЯ МЕТОДОЛОГИЯ И.И. МЕЧНИКОВА И СОВРЕМЕННАЯ АДРЕСНАЯ ИММУНОКОРРЕКЦИЯ ПРИ МИАСТЕНИИ

30-37

Климова Е.М., Дроздова Л.А., Лавинская Е.В., Быченко Е.А.

INTEGRATED METHODOLOGY OF I.I. MECHNIKOV AND MODERN ADDRESS IMMUNOCORRECTION AT MYASTHENIA

Klimova E.M., Drozdova L.A., Lavinskaya E.V., Bychenko E.A.

Introduction. There is carried out reconstruction of the past in the field of integrated discoveries of well-known scientist I.I. Mechnikov for research of aspects of phagocytic function of immune cells and infectious factors in etiology and pathogenesis of progressing myasthenia. There are analyzed the leading factors which have generated scientific outlook and integrated analytical methodology of knowledge of I.I. Mechnikov – the native of the Kharkov province, the graduate student of the Kharkov Imperial University of 1864, the Nobel prize winner of 1908 for creation of the theory of phagocytosis and the author of set of works in the field of microbiology, immunology and virology.

Material & methods. The work studied the mechanisms of disorder of various stages of barrier phagocytic function of neutrophils and frequency of occurrence and various degree of expression of virus persistence at patients with myasthenia is determined. Phagocytosis disturbance leads to uncontrollable development of infections at myasthenia. Advance of muscular delicacy and morph-functional disturbances in thymus, obviously, depend on the individual mechanisms which affect various stages of immune disbalance. The whole century has passed from the moment of creation of the phagocytic theory. For this time all stages of this process have been studied, methodical approaches are developed for an estimation of specific features of this phenomenon, from light microscopy to flowing cytofluorometry. Possibilities of light microscopy allow to visualize the stages of phagocytosis from chemotaxis and adhesions to completeness of digestion by neutrophils in dynamics. And Nitro Blue Tetrazolium Reduction Test (NBTR) is used for an estimation of enzymatic activity of phagocytes for initiation of formation of active forms of oxygen at the phagosoma formation stage. The given method allows to investigate stages of oxygen-dependent metabolism of neutrophils. Along with these methods of estimation of phagocytosis, which don't always give the high-grade information about functional condition of phagocyte leucocytes, it is expedient to apply a fluorescent method with use of acridine orange (AO).

Results & discussion. Accruing digestion of yeast cells by lysosomal enzymes of neutrophils destabilizes DNA and facilitates its denaturation with respective alteration of a spectrum of a luminescence of yeast – red colour ($\lambda_{max} = 640$ nanometers). Undigested yeast keeps the native form of DNA, that is green colour. The visual estimation of chemotaxis, adhesion and endocytosis has allowed to estimate quantity of phagocyte cells. The phagocytic index was up-to-date of referential values at M and MT. The minimum value of endocytosis of neutrocytes was revealed in MG group. Insufficiency of digesting ability of neutrophils can lead to negative consequences, if neutrocytes migrate in various tissues of an organism with undigested antigens. The low digesting activity of granulocytic neutrophils has been revealed at patients with MT (the yeast, which didn't expose digestion, kept the native form of DNA and, accordingly, they have green luminescence of constant intensity and light-orange colour). Results of immunofluorescence

correspond to data of visual observation of adhesion and endocytosis of phagocyte neutrophils (the first methodical approach – light microscopy). The low intensity of formation of active forms of oxygen has been revealed in the NBTR-test according to intensity of oxidation-reduction reactions. The low oxidising reserve of enzymes of neutrophils has been revealed in induced NBTR-test at MG because at this category of patients the spontaneous level of oxidation was in 4 times more than induced one. High frequency and antigenic virus load (CMV) has been revealed at patients with MT, and maximum persistence VEB has been revealed at MG. Research of presence and processing of antigens, functional oxygen-dependent activity of enzymes of neutrophils and completeness of phagocytosis has revealed various degree of disturbances of barrier function of phagocyte cells, and also change of the titer and frequencies of occurrence of herpes viruses CMV and VEB at various clinical phenotypes of myasthenia.

Conclusion. It is shown, that degree of expression and frequency of occurrence of persistence of cytomegalovirus and Epstein-Barra virus are interconnected with defects of various stages of phagocytosis, its completeness and activity of the intracellular enzymes which participate in formation of active forms of oxygen, and intensity of formation of monomers of DNA of the microorganisms which are grasped by phagocytes. Disturbance of barrier function of immunity at myasthenia is significant for a debut and disease advance. An estimation of phagocytosis and virus persistence, as trigger factor of myasthenia, is important for a choice of target therapy. Use of evolutionary scientific methodology of I.I. Mechnikov in the synthetic approach for diagnostics of trigger factors and monitoring of stage of formations of pathological process allows to prove individual medical-diagnostic algorithm for correction of various clinical forms of autoimmune diseases. The approaches for address therapy are proved at various clinical phenotypes of myasthenia which includes carrying out of staged monoligand therapy by peptides and enzymes. This therapy referred on activation of intracellular enzymes of neutrophils at incompleteness of phagocytosis, and application of the immunoglobulins which are specific to herpes viruses.

Key words: myasthenia, barrier function, viral persistence, immunotherapy

ТАКТИКА МЕДИКАМЕНТОЗНОЙ ТЕРАПИИ ПАЦИЕНТОВ С БОЛЕЗНЬЮ, ВЫЗВАННОЙ ВИРУСОМ ЭБОЛА 38-41

Бондаренко А.В., Гвоздецкая М.Г., Зоц Я.В.

MANAGEMENT OF THE PATIENTS WITH EBOLA VIRUS DISEASE

Bondarenko A.V., Hvozdetzka M.G., Zoc Ya.V.

The largest in the history of the Ebola virus disease (EVD) outbreak was recorded in 2014. There are 9976 lethal cases from 24282 infected people (data up to 8 March 2015) within a year from the time of its announcement in West African countries. The outbreak started in Guinea then spread to neighbouring Sierra Leone and Liberia across land borders, to Senegal and Mali by ground transportation, and to Nigeria, Spain, United States of America and the United Kingdom by air transport. If in the previous years disease was the problem of endemic countries in Central Africa nowadays it became a major medical and social problem all over the world. The effective licensed drugs for the treatment and prevention of the disease does not currently exist, experimental drugs (ZMapp, TKM-100802, AVI 7537 Sarepta, Favipiravir T705, BCX4430 Biocryst, Brincidofovir, Nano Silver et al.) are extremely limited, and they are still under investigation. Evidence their effectiveness is suggestive, but not based on solid scientific data from clinical trials. Safety is also unknown. There is consensus that the hyperimmune globulin or convalescent plasma containing high titres of specific neutralizing antibodies to Ebola virus, which leads to decrease the viral load in the blood, is considering to use in an epidemic area as a matter of priority. Experience has shown that the risk of EVD importation into Ukraine remains high despite all preventive measures. Thereby health care providers should be prepared to confront this problem and know how to manage the symptoms of the disease. The management of the patients with EVD mainly should be aimed to early recognition of severe disease and its complications, in combination with appropriate symptomatic therapy. Health care workers should pay careful attention to standard precautions and wear special protective clothing, including goggles, masks and gloves while providing clinical care. Management of intoxication, dehydration, bleeding and shock is a basic and is carried out by common methods. Management of the pain syndrome and anxiety is especially important too. Ribavirin is recommended for the treatment of the patients with Lassa fever and CCHF and it does not apply to the Ebola and Marburg viruses. In most cases, it is impossible to make the diagnosis based only on epidemiological anamnesis and clinical symptoms due to the absence in Ukraine of laboratory express diagnostics kits. Ribavirin should be given empirically to all patients with suspected EVD and other viral haemorrhagic fevers considering difficulties of the differential diagnosis at early stage of infection, especially in pregnant women, due to extremely high maternal and fetal mortality associated with Lassa fever despite on drug adverse effects. All patients should be screened for malaria considering common signs of the EVD clinical manifestations and tropical malaria, antiparasitic therapy should be given to those with a positive result of the research. The intensive supportive care for EVD is the same time for the septic shock due to bacterial infections and malaria. Intensive supportive care is the only clinical management that can be provided to these patients and may have a positive impact on disease outcome. The treatment of the shock should be comprehensive and aimed to maintain vital functions. Broad-spectrum antibiotics should be given empirically during the first hour of the shock therapy. Choice of antibiotics depends on presence of signs of local infection, local disease patterns, and availability of antibiotics. Thus, management of EVD should be based on a set of measures such as clinical management, surveillance and contact tracing, high-quality laboratory services, safe burial and social mobilization.

РОЛЬ МІКРОФЛОРИ ДИСТАЛЬНИХ ВІДДІЛІВ КИШКОВОГО ТРАКТУ В ПІДТРИМЦІ ОКСАЛАТНОГО ГОМЕОСТАЗУ 42-46

Осолодченко Т. П., Лук'яненко Т. В., Андреева І. Д., Волянський Д. Л., Штикер Л. Г., Козубова Г. М.

ROLE OF THE MICROFLORA IN DISTAL INTESTINAL TRACT BY MAINTAINING OXALATE HOMEOSTASIS

Osolodchenko T.P., Lukyanenko T.V., Andreieva I.D., Volyanskiy D. L., Shtiker L. G., Kosubova H. M.

Human intestinal microflora is part of the human body and performs numerous function. Considerable research interest is in the field of probiotics for the prevention of kidney stones, which is one of the most common urological diseases. Urolithiasis is one of the most common urological diseases. This is polyetiological disease congenital and acquired character with complex physical and chemical processes that occur not only in the urinary system, but also the whole body. None of the treatments does not guarantee full recovery of the patient and often leads to relapse. The open methods of removal stones yield news minimally invasive the technologies. Development of stone formation depends on the presence of many factors, metabolic disorders, chronic urinary tract infections, genetic disorders and more. Most have the following metabolic disorders as hypercalciuria, hiperurikuria, hipotsytraturia, hyperoxaluria and hipomahniuria. Among all types of urolithiasis kaltsiyoksalatny ranked first in the prevalence rate - about 75.0 - 85.0 % of cases. Dietary restriction by oxalates is the unreliable method of preventing disease. Although there is evidence for the growth inhibition normobiosis representatives, which in turn enhances the absorption of salts of oxalic acid oxalate in the application of sodium, magnesium and cobalt in their intragastric administration. Recently published many papers on the impact on the level of oxalate intestinal microflora. The first publications appeared on the influence of gram-negative obligate anaerobes *O. formigenes* the concentration of oxalate in the urine. This anaerobic bacteria living in the colon, its prevalence - 46.0 % - 77.0 % of the adult population. *O. formigenes* reveals the symbiotic

interaction with the human body by reducing absorption of oxalate in the intestinal cavity with subsequent decrease in their concentration in plasma and urine. *O. formigenes* has two key enzymes - oksalyl - koadecarboxylase and formyl - koatransferase performing metabolic conversion of oxalate in the cavity of the colon. The polymerase chain reaction has advantages over previously adopted methods - culture and photometric in the diagnosis of the presence of *O. formigenes*. The taking of antibiotics reduces of *O. formigenes* in the colon. The microorganism is resistant to amoxicillin, ceftriaxone, vancomycin and is sensitive to ciprofloxacin, clarithromycin, azitromycin, clindamycin, doxycycline, gentamicin levofloxacin, tetracycline and metranidazol. In the metabolism of oxalate involved and other microorganisms. There are studies that prove the value of other taxonomic groups oxalate degradation: *E. coli*, *Lactobacillus spp.* There is the concept that the use of probiotics is capable of degradation of oxalate in the gut and reducing their absorption in the gastrointestinal tract. There is investigated microbiological method for the treatment of urolithiasis and hyperoxaluria through the use of probiotic *O. formigenes* (at the stage of clinical trials). This method is not traumatic, it can be efficient, cost-effective and environmentally safe. Implicitly that *Lactobacillus spp.* and *E. coli*, along with *O. formigenes*, are promising targets for further research and their application in the field of biotechnological production. To improve the efficiency and expanding the range of their application further work in search and development of new probiotics, given the requirements for food and pharmaceuticals that will effectively dostato prevent or reduce the number of recurrent stone formation.

Keywords: urolithiasis, calcium oxalate, hyperoxaluria, probiotic, *O. formigenes*, *E. coli*, *Lactobacillus spp.*

ЕКСПЕРИМЕНТАЛЬНІ РОБОТИ (EXPERIMENTAL STUDY) ФАРМАЦІЯ (PHARMACY) ФАРМАКОГНОЗІЯ (PHARMACOGNOSY)

STUDY OF ORGANIC ACIDS IN ALMOND LEAVES

47-50

Lenchyk L. V., Samaneh Bayat, Kyslychenko V. S.

Introduction. Almond (*Amygdalus communis*) is a stone fruit, from the *Rosaceae* family, closest to the peach. It is spread throughout the entire Mediterranean region and afterwards to the Southwestern USA, Northern Africa, Turkey, Iran, Australia and South Africa. It is sensitive to wet conditions, and therefore is not grown in wet climates. Iran is located in the semi-arid region of the world. Because of its special tolerance to water stress, almond is one of the main agricultural products in rainfed condition in Iran. Almond leaves have been investigated for their phenolic content and antioxidant activity. It was found that total antioxidant activity and phenolic compounds exhibited variations according to season, plant organ (leaf and stem) and variety. Analysis of previous research on almonds focused on investigating compounds mostly in seeds and phenolic compounds in leaves, but organic acids in leaves have not been studied. Aim of this study was investigation of organic acids in leaves of almond variety which is distributed in Razavi Khorasan province of Iran.

Materials and Methods. In August 2012 almond leaves were collected in Iran, dried and grinded. The study of qualitative composition and quantitative determination of carboxylic acids in almond leaves was carried out by gas chromatography with mass spectrometric detection. For determination organic acids content, to 50 mg of dried plant material in 2 ml vial internal standard (50 µg of tridecane in hexane) was added and filled up with 1.0 ml of methylating agent (14 % BCl₃ in methanol, Supelco 3-3033). The mixture was kept in a sealed vial during 8 hours at 65 °C. At this time fatty oil was fully extracted, and hydrolyzed into its constituent fatty acids and their methylation was done. At the same time free organic and phenolcarbonic acids were methylated too. The reaction mixture was poured from the plant material sediment and was diluted with 1 ml of distilled water. To extract methyl esters of fatty acids 0.2 ml dichloromethane was filled up, gently shaken several times within an hour and then obtained methyl esters extract was chromatographed. Injection of sample (2 µl) in a chromatographic column was carried out splitless, which allowed introducing the sample without flow division and significantly (10-20 time) increased sensitivity to chromatography analysis. Content of organic acids were determined on Agilent Technologies 6890 chromatograph with mass spectrometric detector 5973; chromatography column - INNOWAX, capillary diam. 0.25 mm and a length of 30m; the rate of carrier gas (helium): 1.2 ml/min; heater temperature - 250°C; thermostat temperature was programmed from 50 to 250 °C with a speed of 4 °C / min. For components identification, library of mass spectra NIST05 and WILEY 2007 with a total number of spectra more than 470,000 in conjunction with AMDIS and NIST programs were used. The statistical processing of results was carried out using package Statistica 6.0. The error does not exceed 5%.

Results and discussion. 32 organic acids were established in almond leaves and their quantitative values were determined, using internal standard method. Overall, plant raw material contained 1.80% of the organic acids, including (%) – 0.75 fatty; 0.95 di- and three carboxylic; 0.10 phenol carboxylic acids. Among the carboxylic acids, oxalic and malic acid were the largest with- 3616.41 (38.23%) and 3343.03 (35.34%) mg / kg, respectively. Palmitic and linoleic acids dominated among the fatty acids, their content was determined as (mg/kg) 2343.49 and 1963.60 that were 30.98 % and 25.96% respectively of the total fatty acids. Among phenol carboxylic acids, the largest content was defined for benzoic acid. It was 488.43 mg / kg or 50.16% of the total amount of phenol carboxylic acids.

Conclusion. Almond leaves were investigated by gas chromatography. 32 organic acids were established and their quantitative value were determined. It was found that almond leaves contain 1.80% of the organic acids, including (%) – 0.75 fatty acids; 0.95 di- and three carboxylic acids; 0.10 phenol carboxylic acids. The results of this study are significant for determining beneficial compounds in almond leaves, so making use of these plant raw material as source of new medicines in the future is possible.

Keywords: almond, leaves, gas chromatography, organic acids.

PHYTOCHEMICAL STUDY OF COSMETICS FOR HAIR COLORING

51-56

Pietrzyk D., Paradowska K., Wawer I., Diakonova Ia.

Introduction Henna-based cosmetic products are becoming increasingly popular. They can be used during pregnancy, lactation as well as for temporary children's tattoo. The aim of this work is to develop quality control methods, allowing determining the naturalness of the composition of hair coloring cosmetic products, as well as the presence of lawsone and its quantitative content.

Material & methods The researched objects were eight hair coloring cosmetic products. The spectrophotometer UV-vis Evolution 60S was used in our phytochemical studies. The quantitative content of chlorophyll *a* and *b* was determined in methanolic extracts by spectrophotometric method, using the methodology proposed by K. Miazek. By using well-known methods, methanolic and aqueous extracts were obtained from the studied objects. The extracts, then, were purified to obtain dry residues containing lawsone. Hair color pastes were obtained according to the instructions on the packages of researched products, and finally chloroform extracts were obtained from these pastes. Quantitative content of lawsone in methanolic and aqueous extracts and dry residues after cleaning of the extracts were

determined by the spectrophotometric method. The wavelengths at which the solution of lawsone gives absorption maxima were determined experimentally on the basis of the spectra of the standard sample of lawsone dissolved in methanol (methanolic extracts) and in water with the addition of aqueous NaHCO₃ (aqueous extracts). The quantitative content of polyphenolic compounds in methanolic and aqueous extracts of the researched objects in terms of gallic acid was performed by the spectrophotometric method at the wavelength of 765 nm using the technique of Folin - Ciocalteau. The gallic acid (by virtue of absorbance dependence on concentration) was used as a standard sample to construct the calibration graph.

Results & discussion The total content of chlorophyll in the samples was determined by spectrophotometric method. The resulting calculated ratio of chlorophyll *a* to chlorophyll *b* for researched objects 1-8 was 1 - 2.35, 2 - 2.0, 3 - 4.05, 4 - 3.76, 5 - 4.29, 6 - 0.28, 7 - 0.21, 8 - 0.19, respectively. However, the samples 1-5 contain substances of a plant origin. Quantitative content of lawsone in the methanolic extracts of samples 3, 4, 5 was 3.9, 4.5%, 5.9%, respectively, at the wavelength of 249 nm and 3.7%, 4.3%, 6.7%, respectively, at 275 nm. Quantitative content of lawsone in aqueous extracts (without adding NaHCO₃) of samples 3, 4, 5 was 6.5%, 5.2%, 5.8%, respectively, and 9.2%, 8.6%, 7.9%, respectively, for aqueous extracts with the addition of NaHCO₃. Quantitative content of lawsone in the dry residues after extraction with methanol and subsequent purification in samples 3, 4, 5 was 3.9%, 1.7%, 3.5%, respectively. Quantitative content of lawsone in the dry residues after water extraction and subsequent treatment in samples did not change. The highest content of polyphenolic compounds (in mg/g) found in the methanolic extracts of samples 8, 5, 4 and 3 was 83.3, 71.1, 65.2 and 59.3, respectively. The lowest content of polyphenolic compounds was found in aqueous extracts with the addition of NaHCO₃ solution of researched objects 7 and 2, amounting 6.8 and 13.7, respectively.

Conclusions . Based on the ratio of chlorophylls *a* and *b* in the researched objects, it was concluded that the samples 1-5 contain components of plant origin. Spectra of aqueous extracts of the samples cannot be used for qualitative determination of lawsone, while the spectra of methanolic extracts can be used only as an auxiliary means, because they do not provide a definite answer. The measurement of the concentration of lawsone in the aqueous and methanolic extracts by spectroscopic method does not give plausible results, as these extracts (except lawsone) contain substances that have their own absorption at the same wavelengths as lawsone. This method can be used to quantify lawsone only after purification of the extracts. The results of this phytochemical study of cosmetics for hair coloring can be used to establish quality control methods for this type of products.

Keywords: lawsone, hair coloring, phytochemistry, spectrophotometric method

СУДОВА ФАРМАЦІЯ (JUDICIAL PHARMACY)

АНАЛІЗ АСОРТИМЕНТУ ЛІКАРСЬКИХ ЗАСОБІВ ДЛЯ ФАРМАКОКОРЕКЦІЇ АЛКОГОЛЬНОГО ТРЕМОРУ В СТРУКТУРІ АБСТИНЕНТНОГО СИНДРОМУ АЛКОГОЛЬНОЇ ЗАЛЕЖНОСТІ

57-64

Шаповалов В.В. (мол.), Шаповалова В.О., Шаповалов В.В., Сосін І.К., Шувера О.В.

ANALYSIS OF THE RANGE OF MEDICINES FOR THE PHARMACEUTICAL CORRECTION OF THE ALCOHOL TREMOR IN THE STRUCTURE OF ABSTINENT ALCOHOL DEPENDENCE SYNDROME

Shapovalov V.V. (Jr.), Shapovalova V.A., Shapovalov V.V., Sosin I.K., Shuvera E.V.

Established that the use of psychoactive substances may lead to premature death. The most commonly used psychoactive substance is alcohol. The authors had previously been justified and suggested for implementation in the practice of medicine cupping method alcoholic tremor in the structure of withdrawal symptoms in alcohol dependence. The article presents an analysis of drugs for the pharmaceutical correction of the alcoholic tremor in the structure of withdrawal symptoms, which are included in the patent of the pharmaceutical correction for the alcohol dependence. According to the international ATC classification included 5 ATC codes clinical and pharmacological groups: "A", "B", "C", «N», «S». The analysis found that in circulation in the pharmaceutical market of Ukraine for the pharmacotherapy of alcohol dependence are mainly domestic remedies (23 pharmaceutical manufacturer) that provide the range of nosology at 88.0%. The next step in the analysis was to determine the types of dosage forms used for the pharmacotherapy of alcohol dependence. Found that the dosage means presented in the form of injection solutions and infusion (36.0%), powders for the preparation of solution (suspension) for ingestion (36.0%) in the form of tablets or capsules (28.0%). At the last stage analyzed registration certificates and found that the registration for the medicines for pharmacotherapy of alcohol dependence are 2015 four international nonproprietary names (8 drugs) until 2019 in 4 international nonproprietary names (11 drugs).

Keywords: medicines, assortment, alcohol dependence, pharmaceutical correction.

ВИМОГИ ДО ЗБЕРІГАННЯ І ТРАНСПОРТУВАННЯ БІОТЕХНОЛОГІЧНИХ ЛІКАРСЬКИХ ЗАСОБІВ ЗГІДНО З ДІЮЧОЮ НОРМАТИВНОЮ БАЗОЮ МОЗ УКРАЇНИ

65-69

Шукаєва О. П.

REQUIREMENTS FOR STORAGE AND TRANSPORT OF BIOTECHNOLOGICAL MEDICAL PRODUCTS IN ACCORDANCE WITH THE REGULATORY FRAMEWORK OF MINISTRY OF PUBLIC HEALTH OF UKRAINE AND DETECTION OF VIOLATIONS IN THE MEDICAL AND PHARMACEUTICAL INSTITUTIONS

Shukaeva O.

Introduction. The rapid development of the pharmaceutical industry and the expansion of the range of biotech drugs require special conditions to ensure the quality, storage and transport through out the entire chain: manufacturer - distributor - pharmacy - hospital - the patient. We analyzed the current legislative frame work of Ministry of Public Health of Ukraine and conducted a study to identify and analyze of typical violations in the medical and pharmaceutical institutions. The aim of the investigation was to investigate and analyze inspection acts under storage and transport of biological medical products and identify major violations during the performance requirements for storage and transportation of drugs, level of awareness about medical products which are requiring special storage requirement.

Methods: systemic, logistical, structural, marketing, regulatory.

Results & discussion. According to the data presented in the report «Assessing biosimilar uptake and competition in European markets» of «IMS Health», sales of medical products with biological nature - biological medicinal products and biosimilars is about 27% of total sales of drugs in the EU. This segment of the pharmaceutical market is characterized by faster growth compared to the pharmaceutical market as a whole. Thus, in 2012-2013 years sales of biological medical products in the EU countries increased by 5.5% compared to 1.5% increase in total sales of drugs. It is important that in Europe, according to the 2013 preparations, the market share in value terms, with eight to prepare biological products, the term of patent protection that are either already expired or will expire by 2020, and therefore they can be competitors with biosimilars. In creating the number of medications on the market requires a careful approach of storing and preserving the quality of distribution during throughout the life of the medical products in the chain: manufacturer - distributor - pharmacy - health care setting - patient. The percentage of major flaws in the system supply thermally labile pharmaceutical products related to violation of temperature regimes average 35 to 43%.

Conclusion. Assessing the overall state of the organization, storage, transportation and complying with the requirements of "cold chain"

for Ukraine should be noted that, despite some progress in this area a lot of works to be performed at all levels of health care are needed. Necessary to improve practices in the training of personnel, development of modern refrigeration equipment and means of objective control, organization of manufacturing and to provide all the equipment manufacturing for enterprises, and public health institutions and pharmacies. Need to review the functional responsibilities of pharmaceutical workers in order to strengthen the responsibility for dispensing of biotechnological medical products.

Keywords: biotech drugs, regulatory documentation, storage, transportation.

ТЕХНОЛОГІЯ ЛІКІВ (TECHNOLOGY OF DRUGS)

РОЗРОБКА СКЛАДУ ІНФУЗІЙНОГО ПРЕПАРАТУ НА ОСНОВІ МОКСИФЛОКСАЦИНУ 70-73 Алмакаєва Л.Г., Бєгунова Н.В., Науменок Л.Г., Доля В.Г., Алмакаєв М.С.

DEVELOPMENT OF COMPOSITION OF INFUSION MEDICATION ON BASIS OF MOXIFLOXACIN

L.G. Almakaeva L.G., Begunova N.V., Naumenok L.G., Dolya V.G., Almakaev M.S.

Application of fluoroquinolones covers by experience of treatment more than 800 million patients, and presently they are one of basic classes in the antimicrobial arsenal of practical medicine. Such achievements became possible after the clear understanding of intercommunication of structure and activity of molecules of this class of antibiotics. This knowledge became the basis for the synthesis of new derivatives with a wide range, powerful activity and improved pharmacokinetic profile for the best clinical outcome.

Moxifloxacin is 8-methoxyfluoroquinolone of wide spectrum which interacts mainly with DNA gyrase of gram-negative and with topoisomerase of IV type of gram-positive bacteria. He has the extended activity against gram-positive cocci, however keeps activity against gram-negative bacteria. Moxifloxacin also has good activity against atypical respiratory pathogens (*Legionella pneumophila*, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*). Another his feature is high anti-anaerobic activity. Therefore development of domestic medication with Moxifloxacin - a fluoroquinolone 4 generations - is actual.

Materials and methods

Research material was a substance of Moxifloxacin hydrochloride, produced by firm «Sansh Biotech Pvt. Ltd.», India, a dosage form on the basis of Moxifloxacin - solution for infusion. Qualitative and quantitative control of samples of the drug were conducted on parameters which characterize stability: pH, content of active substance, transparency, colour, related impurities, mechanical inclusions on methods, which are described in SPhU.

Results and Discussion

Proposed the drug is antibiotic of wide spectrum of action of fluoroquinolone. Moxifloxacin hydrochloride is powder pale yellow with slightly hygroscopic nature. He moderately dissolve in water and methanol, poorly will dissolve in hydrochloric acid and ethanol, and practically will not dissolve in an acetone and toluene. pH 0,2 % solution is in a range 3,9 – 4,6. Active substance enters in comparison drug in the concentration of 1,74 mg/ml or 0,174 %. Thus, solubility of it suffices for the receipt of water solution of necessary concentration without fallouts of precipitation or appearance of suspension and opalescence from insufficient solubility. Also, is not the necessity of addition of auxiliary substances - solubilizers for the increase of solubility. For achievement of necessary level of osmolarity and isotonicity in the complement of preparation was entered sodium chloride which is classic used for these aims. Concentration of sodium of chloride as well as in medication analogue Avelox IV® is determined 8 mg/ml. By us the optimum pH range was confirmed for solution of preparation «Moxifloxacin 400 mg, solution for infusion in-bottle 250 ml» within the limits of 4,1-4,6. At preparation of solution it is recommended to correct him pH addition of alkaline and acid agents, indicated in composition, is 1M solution of hydrochloric acid and 2 M sodium hydroxide

Conclusions

Rational composition of infusion medication on the basis of Moxifloxacin was theoretically grounded on the basis of study of literary information and physical and chemical and technological properties of substance of Moxifloxacin hydrochloride and experimentally confirmed. The optimum the limit of pH solution was defined for the receipt of stable dosage form of solution for infusion on the basis of Moxifloxacin. 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: Moxifloxacin, pharmaceutical development, pH range.

ОБГРУНТУВАННЯ ТЕМПЕРАТУРНОГО РЕЖИМУ ВИГОТОВЛЕННЯ СУПОЗИТОРІВ З 74-79 ГЛІФАЗИНОМ

Дмитрієвський Д.І., Куцанян А.С., Гербіна Н.А.

JUSTIFICATION OF TEMPERATURE CONTROL FOR PRODUCTION SUPPOSITORIES WITH GLIFAZIN

Dmitrievskiy D.I., Kutsanyan A.S., Gerbina N.A.

The intensive search for new anti-diabetic drugs, carried out in the National pharmaceutical university in recent years led to the creation of complex drug "Glifazin" on base of which the composition and technology of suppositories with hypoglycemic effect were developed. Now comprehensive physicochemical and pharmacological study of the dosage form are going on. This paper presents results of determining the critical parameters of technology of suppositories with Glifazin produced by molding - temperature control of homogenization and molding of suppository mass. This mode, as shown in the work, grounded on the analysis of rheological behavior of the system in the temperature range in which it is the transition from the liquid state of Newtonian type flow to the plastic-bound state of non-Newtonian flow type. This interval for suppository mass with Glifazin is in the range 45-60 °C.

Materials and methods. As the object of the study the suppositories with Glifazin 0.1 g and polyethyleneoxide base on which they are prepared were taken. The study of structural and mechanical (rheological) properties of suppository base and suppository mass were performed on a rotary viscometer «Reotest-2» (Germany) with coaxial cylinders and the temperature range 45-60 °C. Determination of hardening temperature, resistance of suppositories to decay and their dissolution time were measured by methods of the State Pharmacopoeia of Ukraine. Determination of uniformity suppository mass was assessed by quantitative content of Glifazin in selected samples by using UV spectrophotometry method at 271 nm against a standard sample of Onozid.

Results and discussion. The analysis of rheogram shows that the suppository mass with Glifazin in the test temperature range has falseplastic type of flow. The presence of hysteresis loops indicates that this system has dispersed thixotropic properties. Thus, an increase in temperature leads to a decrease in the area of the hysteresis loop and at 60 °C type flow close to Newton. Adding of Glifazin into a suppository basis significantly changes its reoparameters - increases structural viscosity and increases thixotropic properties of system, due to the influence of the concentration of solids in the system, resulting in reduced her mobility. So important when justifying production technology suppositories is an optimal temperature casting of suppository mass. Other important technological factors whose influence was investigated in this study were speed and time of mixing suppository mass. The result of the research was the study of temperature, speed and time of mixing of suppository mass that is moving but, because of the structuring system started, the processes of

sedimentation of solid phase is not occurring, and suppositories prepared in all respects comply with State Pharmacopoeia of Ukraine.

Conclusions. 1. The structural and mechanical properties of suppository polyethylenoxide bases and suppositories with vegetable substance Glifazin in the temperature range from 45 °C to 60 °C were studied. 2. Influence of temperature, speed and time of mixing suppository mass on the rheological properties and basic properties of Pharmaceutical Manufacturing suppositories were studied. It is shown that homogenization of suppository mass with the rotation speed mixers 0.9 s⁻¹ at 55 °C for 1 h gives a suppository that meet the requirements of SPU. 3. On the basis of the data obtained reasonable basic technological parameters of suppositories with Glifazin were proposed: homogenization temperature (55 °C) temperature dosing (52-53 °C), frequency (0.9 s⁻¹) and the mixing time (30-60 min). The results of studies were used in the development and standardization of technology rectal suppositories Glifazin to treat diabetes type 2.

Keywords: suppositories, diabetes, Glifazin, technology, temperature, rheology.

МЕДИЦИНА (MEDICINE) ВІРУСОЛОГІЯ (VIROLOGY)

INFECTIOUS MONONUCLEOSIS IN CHILDREN AND WAYS OF IMPROVEMENT THE TREATMENT OF PATIENTS

80-83

Olkhovska O.M.

Introduction. The beginning of this century is characterized by an epidemic of herpesvirus infections, whose frequency and spread continue to rise. Infection by the herpes virus group occurs mainly during the first five years of life and leads to life-long persistence. Despite the similarity of clinical features of the syndrome of infectious mononucleosis (IM) caused by cytomegalovirus, human herpes virus type 6 and Epstein-Barr virus (EBV), pathogenic differences occurring in the body should be realized. Despite the presence of specific antiviral drugs up to the date, scientists haven't managed to reduce pathogen circulation in the human population and to achieve absolute elimination of the virus from the body of an infected person. Questions about the use of nonspecific antiviral and «immunomodulatory» drugs against herpes virus infections get a mixed response. The purpose of the study was to examine the efficacy of interferon in the treatment of children with IM.

Materials and methods. At the Regional Children's Hospital of Infectious Diseases, Kharkiv the comparison of the dynamics of clinical and laboratory parameters of 102 children in the age 1-5 years with moderate tonsillar-glandular form of IM was conducted. The diseases were caused by EBV. The control group consisted of 58 children whose treatment was performed in accordance with generally accepted schemes of existing protocols for diagnosis and treatment of infectious diseases in children. The main group contained 44 patients, which had a complex therapy with the combination of recombinant interferon alpha-2 Viferon-Fearon at doses of 500 000 IU, 2 times a day during 5 days. Our choice of this particular drug was due to the form of drug release - suppositories. In addition, the product contains ascorbic acid and tocopherol acetate, which are powerful antioxidants and membrane-stabilizing factors.

Results and discussion. In the majority of children the disease started acutely with fever, symptoms of intoxication, tonsillitis (lacunar tonsillitis), and the increase in size of submandibular and cervical lymph nodes, difficulty in nasal breathing. At the same time, 22 (21,6%) children had slow onset, which was characterized by catarrhal symptoms and gradual rise in temperature. Serous discharges from the nose, nasal congestion, dry cough that gradually became moist, appearance of "snoring" during sleep were the main catarrhal symptoms. An acute respiratory disease was diagnosed for children at the first visit to the pediatrician, and symptomatic therapy was used during three to five days as a primary treatment. However, the fever persisted, catarrhal manifestations and signs of intoxication intensified, and parents started to pay attention on the neck lumps of. Prolonged fever and swollen lymph nodes were a major cause of hospitalization. Clinical examination of children, who proceeded to the hospital, had revealed the symptoms of tonsillitis. But membranes on the tonsils were found only in 10 patients; the other patients had hyperaemia or "looseness" of the oropharynx mucosa. The ultrasound of the abdomen was conducted for all patients during the hospital stay, which showed an increase in the size of the liver, signs of parenchymal reaction of liver. At the same time, increasing the size of the spleen was observed in 67 patients (65,7%), and in 36 patients (35,3%) signs of hepatosplenitis were found. An increase in aminotransferase levels was found in biochemical analysis of liver samples in 21 children (20,6%), but these figures decreased to physiological norms at the time of discharge from the hospital. Despite the known contraindications on the use of Ampicillin in the treatment for IM, this drug was prescribed for 11 patients (10,8%) in the outpatient basis, which led to appearance of immunocomplex rash with the hemorrhagic component in 2 (1,9%) of them. In peripheral blood leucocytosis ($15,48 \pm 2,78 \cdot 10^9 / L$) and lymphocytosis ($72,66 \pm 3,58\%$), monocytosis ($13,06 \pm 2,31\%$), accelerated ESR ($18,96 \pm 3,22$ mm/h) were found. Only 57 children (55,9%) had abnormal blood mononuclear cells (virocytes), whose number was not high and reached $6,84 \pm 1,67\%$. Patients had thrombocytopenia to $155,49 \pm 13,22 \cdot 10^9 / L$ in 15 cases (14,7%) and anaemia in 19 (18,6%) patients. We analyzed the efficiency of the use of the recombinant interferon in complex treatment, based on a comparative analysis of the dynamics of basic clinical and laboratory parameters of the two groups of patients. Accelerated regression of clinical symptoms and laboratory parameters was found in children, to whom complex therapy with recombinant interferon alpha 2 (Viferon-Fearon) was used. Significant differences in clinical parameters were found in terms of normalization of body temperature ($5,18 \pm 1,12$ vs $7,96 \pm 0,77$ days, $p < 0,05$), elimination of nasal breathing difficulty ($4,06 \pm 0,98$ vs $6,68 \pm 0,82$, $p < 0,05$), reducing the size of the regional lymph nodes ($4,98 \pm 1,11$ vs $7,95 \pm 0,87$, $p < 0,05$) and liver ($7,65 \pm 1,16$ vs $10,98 \pm 1,15$ days, $p < 0,05$). The positive effect of interferon on peripheral blood caused an early normalization of leukocytes and ESR, the last one occurred significantly faster ($7,19 \pm 1,06$ vs $10,42 \pm 1,17$ days, $p < 0,05$). The duration of treatment of the main group in hospital was $9,02 \pm 1,21$ days while the treatment of the control group lasted $12,84 \pm 1,43$ days, $p < 0,05$. Prescription of Viferon made it possible to shorten the hospital stays of patients in approximately 3-4 days.

Conclusions. Thus, one of the most perspective ways to improve the treatment for EBV IM in children is the use of recombinant interferon alpha-2. In addition to positive effects on the clinical course of the disease, the advisability of appointing this drug is due to its probability of development IM in young children alike to respiratory infections. Prescribing Viferon in first hours of the appearing of catarrhal symptoms in children is appropriate, regardless of the results of further definition of the etiology of the disease, because there are many studies that prove the efficacy of interferon for acute respiratory viral infections in children also.

УДОСКОНАЛЕННЯ ТЕРАПІЇ ХВОРИХ НА ГОСТРІ РЕСПІРАТОРНІ ВІРУСНІ ІНФЕКЦІЇ

Копча В.С., Копча Ю.В.

84-90

ADVANCEMENT IN MEDICAL TREATMENT OF PATIENTS WITH ACUTE RESPIRATORY VIRAL INFECTIONS

Kopcha V.S., Kopcha Yu.V.

Introduction. Acute respiratory viral infections are the special group of diseases, which in the structure of infectious pathology firmly occupies one of leading places. The problem of morbidity belongs to the number of leading medical problems not only in Ukraine but also in the whole world. In addition, there is a greater risk of epidemic flashes of acute respiratory infections in the conditions of megapolis with the expressed processes of migration and accumulation of people. Purpose of test – to promote efficiency of patients

treatment with acute respiratory viral infections by complex application of preparation «Extralact» on a background traditional (base) therapy without the use of other antiviral preparations, thoroughly to probe influence on clinical motion of the indicated illnesses, endogenous intoxication and immune status of organism.

Patients & methods. Under a supervision was 60 patients (22 men and 38 women) of young and middle age (hesitated from 18 to 58), which treated oneself concerning ARVI. Determined the indexes of Extralact efficiency: general duration of disease; frequency of development of complications; dynamics of clinical displays; dynamics of laboratory indexes, indexes of endogenous intoxication, and immunological indexes. Patients were randomised on 2 groups: a I group (30 persons – 50,0 %) got treatment of base therapy preparations; the II group (30 patients – 50,0 %) on a background base therapy got preparation «Extralact» for 2 capsules 3 times per days during 5 days.

Results & discussion. Based on the examination of 60 patients with ARVI established following. Addition of base therapy of such patients of extralact in a dose 2 caps. 3 times daily during 5 days was accompanied by a significant advantage compared with only basic therapy on several grounds: the greater the number of patients advancing recovery up to 7 days, most regressed cough, relatively less there were complications. After 5 days of extralact application WBC and relative content of stab neutrophils and lymphocytes is normalized, increased leukocyte index of intoxication, approaching normal values, significantly increases the index shift of leukocytes, significantly reduced lymphocytic index closer to normal. This treatment also provides reduction of immunological disorders detected before treatment. Thus, the statistical weight increases the number of white blood cells and normal lymphocytes, maintained at normal levels of IgA and lysozyme concentrations and normal or even increased levels of IFN- α and IFN- γ . On background application of extralact in a therapeutic dose by-reactions did not arise up.

Key words: ARVI, treatment, extralact.

ШЛЯХИ УДОСКОНАЛЕННЯ ПРОФІЛАКТИКИ ВІТРИНОЇ ВІСПИ СЕРЕД ДИТЯЧОГО НАСЕЛЕННЯ УКРАЇНИ В СУЧАСНИХ УМОВАХ

91-94

Кірсанова Т.О.

WAYS TO IMPROVE PREVENTION OF CHICKENPOX AT CHILDREN OF UKRAINE IN MODERN CONDITION

Kirsanova T.O.

Introduction. Chickenpox (CP) in recent years has tended to steady increase in the incidence of various regions of Ukraine, especially among children. The situation regarding the incidence of PA nowadays, especially among children, determines the relevance of infection and requires the solution of problems in finding the most effective ways to prevent the population of Ukraine against CP.

Purpose: to theoretically justify the introduction of the National vaccination calendar of Ukraine vaccine against CP based on the study of modern epidemiological, clinical and paraclinical features of CP in children of Kharkiv region of Ukraine.

Materials and methods. The analysis of statistical data on the incidence of PA in Kharkiv region and 2780 data from case histories of children aged one month PA-18, admitted to the Kharkiv Regional Hospital of Pediatric Infectious Diseases in the last five years. The diagnosis is established on the basis of characteristic clinical manifestations.

Results and discussion. During the period 2010-2014 epidemiological curve morbidity in children with CP has tended to rise with maximum performance in 2011, prevailed among patients, children who lived in the city. The largest recorded incidence in children under 15 years old, had a tendency to increase the proportion of high school age children. Among dominated diseased children attending organized children's groups (kindergartens, schools), including more than a third part of patients lived in closed children's institutions (orphanages, boarding schools, etc.). Clear seasonal disease was traced to the rise of the autumn-winter period. Monitoring the number of children with CP, admitted to hospital, also showed growth in their numbers. The reason for hospitalization were: pronounced intoxication syndrome, abundant rash on skin and mucous membranes, complicated disease, epidemiological indications. The most affected age groups were children 1-10 years. The disease ran mostly in moderately severe and severe forms. Analysis of clinical data showed that almost all children with acute illness began with symptoms of intoxication, temperature up to 38,0-40°C, headache, some children had vomiting. Rash appeared mostly often by the end of the second day. Items were rash as spots 1-3 mm in diameter, round, pink with sharp edges. Subsequently, they were transformed into papules, vesicles, crusts, which were located on non-infiltrated background skin, usually separately without a tendency to merge. New elements of rash appear after 1-2 days and accompanied by fever. Almost half part of children forming vesicles recorded in the mucous membranes of the mouth, genitals and conjunctiva during 4-5 days. In hemogramma of patients revealed leukopenia, lymphocytosis. A quarter of children with CP occurred complications that are most often developed for third-eighth day of the appearance of lesions regardless of severity of clinical manifestations of the disease. The structure dominated by non-specific complications of skin lesions with the development of inflammatory diseases streptococcal and staphylococcal etiology. The structure of specific complications observed CNS with the development of meningitis, encephalitis and meningoencephalitis.

Conclusions. Over the past five years in the Kharkiv region incidence of children with CP remains high with the major indices among children under 15 years. The most vulnerable are children with organized groups (especially closed children's institutions) residing in the city. There has stable tendency to increasing number of complications, particularly specific. High incidence, frequency and severity of complications dictate the need for mandatory vaccination against CP in children. First of all, in our view, it is necessary to consider compulsory vaccination of children from child care centers closed, and may in the future enter into the National calendar of vaccination of healthy children Ukraine. The use of mandatory vaccination of children against CP will significantly reduce the number of cases of children; reduce the number of complications and economic costs of treatment and rehabilitation of these patients.

Keywords: chickenpox, epidemiology, prevention

ОЦІНКА ПОРУШЕНЬ ВУГЛЕВОДНОГО ОБМІНУ У ВІЛ-ІНФІКОВАНИХ ОСІБ, ХВОРИХ НА ХГС І КО-ІНФЕКЦІЮ ВІЛ/ХГС

95-99

Юрко К.В.

ASSESSMENT OF CARBOHYDRATE METABOLISM DISORDERS IN HIV-INFECTED PERSONS, PATIENTS WITH CHRONIC HEPATITIS C AND CO-INFECTION HIV/HCV

Iurko K.V.

Introduction. Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are characterized by their wide distribution and ability to cause health disorders of the working population, thus causing significant morbidity and mortality worldwide. Ukraine - one of the countries of Europe, leads the sad rating of the number of identified HIV positive and AIDS cases and deaths from the disease. Chronic hepatitis C (CHC) is observed in 60-70% of HIV-infected individuals, due to the common modes of transmission of viruses. Co-infection with HIV/HCV is an important public health problem, since viruses, acting synergistically accelerate the progression of liver disease. HIV accelerates the progression of chronic hepatitis C to cirrhosis and hepatocellular carcinoma, thus increases "liver" mortality. This article discussed the state of carbohydrate metabolism in HIV-infected persons, patients with chronic hepatitis C and patients co-infected with HIV/HCV.

Material & methods. The content of carbohydrate metabolism was determined in 107 patients: with chronic hepatitis C - 36 patients,

with HIV infection - 35 and co-infection with HIV/HCV – 36 patients.

Results. In the investigated patients identified carbohydrate metabolism disorders as an increase in serum glucose, insulin, glycosylated hemoglobin, level of insulin resistance. Glucose in patients of all groups was significantly higher than in control subjects. For example, in HIV-infected persons, it was $(5,16 \pm 0,11 \text{ mmol/l})$ in patients with chronic hepatitis C - $(5,35 \pm 0,15 \text{ mmol/l})$, and in patients co-infected with HIV/HCV – $(5,95 \pm 0,15 \text{ mmol/L})$. The insulin content was also increased in patients of all groups - in HIV-infected persons $9,26 \pm 0,24 \text{ MKOD/ml}$, in patients with chronic hepatitis C - $10,6 \pm 0,89 \text{ mU/L}$, and in patients co-infected with HIV/HCV - $11,9 \pm 0,81 \text{ MKOD / ml}$, respectively. HbA1C levels in HIV-infected individuals was $6,18 \pm 0,14 \%$, in patients with chronic hepatitis C - $6,36 \pm 0,13 \%$, and in patients co-infected with HIV/HCV - $7,05 \pm 0,15 \%$. These values were significantly higher than in the control group $(5,74 \pm 0,17 \%)$. HOMA-IR index in the studied patients was increased as compared with the control subjects, and in HIV-infected persons it was $2,51 \pm 0,21$, in patients with chronic hepatitis C - $2,45 \pm 0,17$ and co-infection with HIV/HCV - $3,16 \pm 0,24$ respectively. The greatest manifestation of disorders of carbohydrate metabolism was in patients with established co-infection with HIV/HCV, and the lowest - in HIV-infected individuals.

Conclusion. The most significant manifestations of disorders of carbohydrate and purine metabolism were observed in patients co-infected with HIV/HCV ($t=20,5$; $p<0.001$), that exceed a specified changes in patients with HCV 1,74 times ($t=11,8$; $p<0.001$) and HIV-infected patients ($t=9,1$; $p<0.001$) 2,25 times.

Key words: chronic hepatitis C, HIV-infection, co-infection HIV/HCV, carbohydrate metabolism.

100-104

ПОКАЗНИКИ МІКРОЕКОЛОГІЇ СТАТЕВИХ ШЛЯХІВ У ХВОРИХ З ПАПЛОМАВІРУСНОЮ ІНФЕКЦІЄЮ

Лісяна Т.О., Пономарьова І.Г., Кондратюк В.К., Коблош Н.Д., Кацалап О.М., Матяшова О.І.

INDICATORS MICROECOLOGY GENITAL TRACT IN PATIENTS WITH HPV INFECTIONS

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Matyashova O.I.

Introduction. In recent years proved the involvement of papillomaviruses in the development of a wide range of diseases, which are based neoplastic processes of precancerous and tumor genesis. Human papilloma virus (HPV) are highly contagious, progressive increase in the incidence of genital tract lesions and high oncogenicity. Proven link between the risk of precancerous disease in patients with HPV and chlamydia infection, viruses (HSV, CMV) and pathogens "new generation". The purpose of this study was to evaluate the state of microbiota and analysis of associative forms of genital tract infection in women with HPV depending on the degree of cervical pathology.

Materials and methods. In order to assess the state microecology cervical cancer in women with HPV infection examined 90 patients. Analysis of the results of bacteriological studies conducted taking into account the nature of pathological changes in the lining of the cervix. In particular, examined 23 women (group I) type of inflammatory disorders of the mucosa, 45 patients (group II) with mild cervical dysplasia (CIN I) and 22 - (third group) with cervical dysplasia moderate severity (CIN II). As a control, examined 25 healthy women. Conducting microbiological analysis and calculation of results was performed according to the order number 535 Ministry of Health from 1985 years and the order number 234 Ministry of Health of Ukraine of 10.05.2007 years. Crops performed by sectoral dense planting on differential - diagnostic culture media, to determine the degree of microbial contamination and to identify the best possible range of aerobic and facultative anaerobic microorganisms. Taxonomic position microorganisms was determined according to the directory Bergey. Diagnosis of herpes, cytomegalovirus, chlamydia, mycoplasmosis, ureaplasmosis and fluorenscent performed by using a set of "Herpes-Scan", "CMV-Scan", "Chlamy-Scan", "Urea-Scan" and "Miko-Scan" (Moscow). HPV infection detected by PCR. Gardnerellessis diagnosed by microscopy by staining smears on Romanovsky with subsequent calculation of "core" of cells, setting amine test, determination of pH. The results of bacteriological studies were subject to statistical analysis by Student's method.

Results. The obtained data indicate that patients of the first group identified changes microecology which was to raise the frequency of registration of mixed infection of the cervix opportunistic gram-positive cocci in combination with viruses, as well as the tendency to reduce the protective microflora. The frequency of associative forms of cervical infection was significant and was 72,7%, ($n = 16$). Women with HPV group II and CIN I and indicators microbiota slightly different from the data obtained in women with inflammatory type of stroke. In the second group of patients with HPV and mild cervical dysplasia tended to increase the level of seeding microorganisms pathogenic properties and increased frequency of diagnosis of infections such as chlamydia, mycoplasmosis, ureaplasmosis and gardnerella. The majority (66,6%, ($n = 30$)) of the second group of patients with HPV and CIN I bacterial flora was located in association with viruses and infectious agents "new generation". For comparison purposes, we examined three groups of women HPV who had cervical dysplasia moderate severity (CIN II). In this group of patients revealed increasing contamination cervical gram-positive coccus, not only, but also enterobacteria. The essential deficit lactobacillus. Compared with the data observed in women with HPV and CIN I, in patients with cervical dysplasia moderate severity (CIN II) revealed increased frequency of diagnosis of HSV, gardnerellez, chlamydia and ureaplasmosis. State microecology cervix in patients with HPV and CIN II is characterized by increased levels of viral infection, increasing the proportion of the total spectrum of microorganisms isolated anaerobic bacteria, Enterobacteriaceae and a significant decrease in contamination of the cervix protective microflora. Found increased frequency of registration associative forms of infection (86,3%, ($n = 19$)). Indicators expression of viral and bacterial associations in the third group of women with exaggerated HPV data obtained in patients with HPV and mild cervical dysplasia.

Conclusions 1. Dependence indicators microecology cervical cytologic changes in the type mucosa. In the group of women with inflammatory type of stroke and mild dysplasia as part of the biological community dominated pathogens herpes or cytomegalovirus infection on the background of increases in expression of gram-positive coccal flora and lack of protective microflora. In the group of women with cervical dysplasia moderate severity recorded a significant increase in the frequency of diagnosis of HPV infection, chlamydia, increasing the share spectrum allocated flora anaerobic bacteria (Gardnerella, mobilyunkus) and a significant decrease in lactobacilli. 2. The differences between the frequency and composition of associations of infectious agents from the state epithelium of the mucous membrane of the cervix. The greatest rate of associative forms of contamination of the cervix (86,3%, ($n = 19$)) was found in women with human papillomavirus infection and cervical dysplasia Stepun medium severity. 3. The data obtained indicate the need for control parameters microecology cervix in women for the purpose of early diagnosis of HPV infection, assess the extent of violations of microbiota and the risk of complications.

Keywords: microbiocaeosis, cervix, HPV, cervical dysplasia

ПАРАЗИТОЛОГИЯ (PARASITOLOGY)

ВИДОВОЙ СОСТАВ МАЛЯРИЙНЫХ КОМАРОВ ХАРЬКОВСКОЙ ОБЛАСТИ. ПРИРОДНЫЕ ФАКТОРЫ РАСПРОСТРАНЕНИЯ МАЛЯРИИ

Газзави-Рогозина Л. В.

SPECIES COMPOSITION OF MALARIAL MOSQUITOES KHARKIV REGION. NATURAL FACTORS OF MALARIA TRANSMISSION

Gazzawi - Rogozina L. V.

Introduction. This article describes the species composition of the dominant Anopheles mosquitoes in the Kharkiv region, the season of their possible effective infection, as well as ongoing anti-malaria activities .

Key words: malaria , mosquitoes, p . Anopheles, epidemiology, census, hydraulic events.

Material & methods. The analysis of entomological and meteorological situation in Ukraine and in the Kharkiv region according to data of the Ukrainian Center of control and monitoring of diseases of the Ministry of Health of Ukraine and Kharkiv regional laboratory center. Collection of material (imaginal and larval) was carried out on the territory of natural and artificial water bodies of Kharkiv region in the period 2013 – 2014. When collecting the material used conventional accounting methods mosquito populations. On the territory of the region under study, we have found 30 species of mosquitoes three genera: Anopheles, Culex, Aedes.

Results & discussion. Epidemiological role of each species of mosquitoes depends on several conditions. Dangerous vector species can only be found in large numbers, a significant percentage of individuals in a population that feeds on the blood of man, having a sufficiently long season activity and a sufficient number of females surviving to age possible maturation of sporozoites in their body. In Ukraine, the major carriers - Anopheles maculipennis, An. m. messeae, An. m. atroparvus, An. claviger, An. plumbeus, An. hyrcanus. Mosquito species registered in the territory of the Kharkiv region are susceptible to currently known types of human malaria parasites . Moreover, the dominant species in terms of urban landscapes are An.maculipennis and An.messeae . These species possess all the qualities necessary to be considered dangerous malaria vector control. They are well infected with the three main types of human parasites. In the study area , in terms of urban landscapes, gonoaktivnye females occurs within 3.5-4 months, and Preimaginal stages in reservoirs - about 4.5 months. The maximum number of species observed in mid-July. Due to the high number of attacks and activity in the summer , as well as the confinement of breeding sites to human settlements , An.maculipennis, An. messeae pose the greatest epidemiological risk.

Conclusion. All of the above demonstrates the improvement of environmental conditions for the spread of malaria : growth of the transporter , the increase in precipitation , temperature longer transmission period of invasion .

Keywords: malaria, mosquitoes p. Anopheles, epidemiology, census, hydraulic events.

ПАТОГЕНЕТИЧНІ МЕХАНІЗМИ ПРИ ХРОНІЧНОМУ НАБУТОМУ ТОКСОПЛАЗМОЗИ

108-113

Кочина С.С.

PATHOGENETIC MECHANISMS OF CHRONIC ACQUIRED TOXOPLASMOSIS

Kotsyna S.S.

Introduction. Toxoplasma gondii is an intracellular protozoan that infects approximately one-third of the world's population. Infection in human generally occurs through consuming food or drink contaminated with oocysts and tissue cysts from undercooked meat.

Although latent infection with Toxoplasma gondii is among the most prevalent of human infections, it has been generally assumed that, except for congenital transmission, it is asymptomatic. Different conditions such as, number of parasite, virulence of the organism, genetic background, sex, and immunological status seem to affect the course of infection The demonstration that Toxoplasma infections can alter behavior, reproductive function in patients has led to a reconsideration of this assumption. During chronic acquired toxoplasmosis (CAT) identified the regularities of changes in the ratio of the immune system and the basal levels of sex hormones available informative methods, which made it possible to evaluate the severity of the flow chart and predict treatment outcome without resorting to complex research methods. Found that the host-parasite relationships and clinical manifestations of chronic toxoplasmosis depend largely on protective and adaptive responses and compensatory abilities of the human body.

Material & methods. 112 patients attended in the 6 Department of Kharkiv Regional Infectious Diseases Hospital №22 (Department of Medical Parasitology and Tropical Diseases of Kharkiv Medical Academy of Postgraduate Education.) in Kharkiv, Ukraine were enrolled in the study. Forty four patients (39,3±4,6%) were male and sixty eight (60,7±4,6%) were female. The age of the patients was 18 till 72 years.

Results & discussion. All of 112 CAT patients had subjective clinical symptoms in various combinations: increased fatigue 99,1 ± 0,9%, headache and tiredness 95,5 ± 1,9%, pain in the liver 88,4 ± 3,1%, bitter taste in the mouth 93,8 ± 2,2%, muscle pain 81,3 ± 3,7% and joint pain 69,6 ± 4,3%. Women complained of painful menstruation (57,4 ± 4,7%), irregular menstrual cycle (85,3 ± 3,4%). In the anamnesis of diseases 10,3 ± 2,8% of women had miscarriages and 27,9 ± 4,2% of women had fetal fading. 47,7 ± 4,7% men complained of the decrease in potency. Objective examination: All of 112 CAT patients had lymphadenopathy, 89,3 ± 3,0% patients had subfebrile temperature, 64,3 ± 4,5% of patients had increased sweating, 53,6 ± 4,7% patients had hypertension, increase in liver size was founded in 21,4 ± 3,8% of patients, skin rashes 10,7 ± 3,0%, spleen was enlarged in 66,9 ± 4,4% of patients. Hormonal status: 59 ± 7,4% men have an increased levels of progesterone, 41 ± 7,4% men have an increased levels of estradiol, 13 ± 5,1% men have an increased levels of testosterone. Women 22±5,0% have an increased levels of testosterone, women 7,0±3,1% have an increased levels of progesterone, 10±3,6% women have an decreased levels of estradiol.

Conclusion. The response of host organism to CAT invasion occurs is not the same. It depends on the initial state protective and adaptive capacity of the organism and the liver diseases. This is one of the determining factors of the host-parasite relationship and clinical manifestations of the disease. Prognostic Criterias that determine adaptive-compensatory capacity of the organism in CAT can be basal levels of estradiol, testosterone and progesterone. Physiological differences between men and women play an important role in determining susceptibility to parasitic diseases. The dichotomy in the incidence and severity of many diseases infectious etiology are a strong arguments that the characteristics of men's physiology and characteristics of women's physiology are the important factors of the determining susceptibility to disease.

Keywords: toxoplasmosis, immune system, sex hormones, clinical manifestations.

Велиева Т.А.

DIAGNOSIS AND TREATMENT OF CHILDREN ECHINOCOCCOSIS

Veliyeva T.A.

The problem of echinococcosis, despite the progress made in its diagnosis and treatment, currently remains poorly understood and highly relevant in pediatric Parasitology. Studies of many authors show that in recent years the number of patients with echinococcosis not only universally recognized endemic foci, but also among people in the European region, including in countries such as Romania, Germany, Austria. However, studies on the prevalence and structure of echinococcosis among children in Ukraine, are not held. Despite the large number of papers devoted to the treatment of echinococcosis, the problem of the treatment of this disease in children is still far from its final decision. Usually offered surgical treatment, which is not possible with multiple lesions of the liver or other organs. All this shows the relevance and importance for practical public health issues for further study of diagnosis and treatment of echinococcosis in children.

The purpose of the study. A comparative analysis of the diagnostic efficacy of X-ray and ultrasound method in the diagnosis of echinococcosis in children.

Material & methods. This work is based on a survey of 39 children with hepatic echinococcosis, were examined at the Department of Medical Parasitology and Tropical Diseases Kharkiv Medical Academy of Postgraduate Education from 2005 to 2015. Boys was 1.5 times greater (59.5%) than girls - 40.5%. Children under five years of age accounted for only 4.0% of all patients, due to their limited contact with the environment when compared with older age. The greatest risk of disease was in the 10-13 years of age, the number of children in the group reached 40.3% of the patients. The vast majority of patients (89.6%) lived in rural areas. In this case, the parents of sick children from the village were engaged in farming, were in personal use livestock, dogs, which probably contributed to the invasion. Very often ill children pas-tuhov, shepherds. 78% of patients had close contact with dogs. Study of the structure of morbidity showed that among children with hydatidosis in 90.8% were found isolated liver, 9.1% - together. In 7.0% of the patients were diagnosed with combined lung and liver.

Results & discussion. Clinical examination of children was carried out by the standard method of inspection and collection history. When collecting anamnestic data have focused on the identification of contact with pets, dates of onset of symptoms. The clinical picture of hepatic echinococcosis diverse and largely depend on the size, location and number of cysts, and the nature of complications. Depending on the stage of parasite development and complications of liver hydatid cysts in our study had a different echographic image. Uncomplicated cyst of the liver in 85.8% of cases was introduced liquid (anehogennoe) form a round or oval with clear smooth contours having at the periphery of the double hyperechoic circuit: inwards - chitin shell echinococcus, outwards from it - the fibrous sheath of the liver; shells separated from each other hypoechoic space. In 7 cases, ultrasound cyst of the liver characterized by the presence in the lumen of the crimped hyperechoic structure - detached shell chitin (floating diaphragm). 3 children under ultrasound liver cyst had a typical double loop around the periphery. In their lumen defines a large number of child cysts. Indicators diagnostic efficacy of ultrasound in the diagnosis of liver echinococcosis were: sensitivity 98.0%, specificity 100%, accuracy 97.6%, which confirms the value of the ultrasonic method in the diagnosis of this pathology.

Conclusion. Children with signs of chronic endotoxemia (weakness, loss of appetite, malaise, fatigue, retarded physical development), as well as allergic reactions in various forms, is necessary to conduct surveys using a minimum of safer and more effective diagnostic methods in order to avoid echinococcosis. This method, in our opinion, is ultrasound, which is available for in outpatient and inpatient settings.

Keywords: echinococcosis, children, diagnosis, treatment, endotoxemia, allergia

ТОКСИКОЛОГІЯ, ФАРМАКОЛОГІЯ, ЕКОЛОГІЯ (TOXICOLOGY, PHARMACOLOGY, ECOLOGY)

БІОХІМІЧНІ МЕХАНІЗМИ СПОЛУЧЕНОГО ВПЛИВУ НА ОРГАНІЗМ ТВАРИН ЕЛЕКТРОМАГНІТНОГО ВИПРОМІНЮВАННЯ ТА ПОЗИТИВНОЇ НИЗЬКОЇ ТЕМПЕРАТУРИ

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Літовченко О. Л., Перцев Д. П., Завгородній І. В., Мітельова Т. Ю., Чеховська І. М., Абрамова Л. П., Векшин В. О.

BIOCHEMICAL MECHANISMS OF MIXED EFFECT OF ELECTROMAGNETIC RADIATION AND LOW POSITIVE TEMPERATURE ON ANIMALS' ORGANISM

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At present, biochemical mechanisms of mixed effects of electromagnetic radiation (EMR) and cold on the body are not adequately studied, so this problem is urgent for modern medicine.

Purpose of study. Establishing pathognomonic criteria and biochemical mechanisms of adverse effect of EMR on the organism of laboratory animals in conditions of cold stress.

Materials and methods. The laboratory subacute experiment was carried out on mature white male rats of WAG line, weighing 190-220 g for 1 month. The animals were divided into 4 groups of 10 animals in each group. The first group was subjected to the isolated action of electromagnetic radiation (frequency 70 kHz, tension 600 V/m) at a comfortable air temperature of $25 \pm 2^\circ \text{C}$. The second group was subjected to the mixed action of EMR and low temperature $4 \pm 2^\circ \text{C}$. The third group served as a control with regard to the first group, and the fourth group - with regard to the second, at air temperature of $25 \pm 2^\circ \text{C}$. Expositions were carried out 5 times a week (for 4:00 every day). To identify changes in biochemical parameters studied during the experiments, blood sampling was performed at the stages of 5, 15, 30 days and urine sampling - at the stages of 15, 30 days in dynamics. Blood serum was used as biomaterial. It was determined the content of malondialdehyde (MDA), conjugated diene, content of SH-groups, superoxide dismutase, ceruloplasmin, cholesterol, high density lipoprotein, low density lipoprotein, very low density lipoprotein (VLDL), triglycerides, atherogenic index was determined, the level of urea, alkaline phosphatase, acid phosphatase, content of chlorides, calcium, magnesium, phosphorus, total protein, glucose, and catalase activity. Renal function was studied by the content of creatinine, cholinesterase, urea, uric acid, chlorides, potassium, sodium, calcium, phosphorus and glucose in urine.

Results and discussion. The findings showed that the isolated action of EMR only led to a change in the activity of catalase and a trend toward an increase in MDA level. Values of lipoprotein profile also did not have reliable changes, but high values of atherogenic index throughout the study showed the negative impact of EMR on lipid metabolism. Reliable changes in liver function tests indicated a disorder of liver detoxification function and possible derangement of protein metabolism. A decrease in creatinine and uric acid in the urine of rats is also evidence of this. The mixed effect of EMR and positive low temperature predetermined deeper violations practically in all components of metabolism, which exhibit low levels of SH-groups and the activity of catalase and superoxide dismutase, an increase in the concentration of ceruloplasmin. The observed increase in VLDL and triglycerides indicated the increase of the processes

of atherogenesis. Acid phosphatase activity increased, increased alkaline phosphatase tends to raise the level of serum phosphorus levels in rats of the experimental group. There were more pronounced changes in the functioning of the liver. The level of urea in the blood serum was reliably increased. In the mixed action of EMR and positive low temperature, the level of uric acid in urine reliably increased, indicating that the development of renal failure in this group of animals, which was also indicated by elevated levels of chlorides in the urine.

Conclusions. 1. The leading biochemical mechanisms of adverse effects of mixed action of EMR and positive low temperature is a disorder of the antioxidant system of blood, lipid metabolism and renal excretory function. 2. The mixed effect of EMR and positive low temperature on the organs and systems was more pronounced compared to the isolated action of electromagnetic radiation. 3. The above determines the need to consider the increase of biological effect of EMR established in the experiment on laboratory animals in the conditions of cold stress, when substantiating hygienic standards, the development and introduction of prophylactic measures into the practice of sanitary supervision.

Keywords: rats, electromagnetic radiation, cold, biochemical effects

ОЦЕНКА ПРОТЕКТОРНОГО ДЕЙСТВИЯ ПРОБИОТИКА И ИММУНОТРОПНОГО ПРЕПАРАТА НА МЕТАБОЛИЗМ ЭКСПЕРИМЕНТАЛЬНЫХ ЖИВОТНЫХ ПОСЛЕ ВВЕДЕНИЯ КСЕНОБИОТИКА

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Звягинцева О.В., Климова Е.М., Лавинская Е.В., Ленкевич А.С.

CHANGING METABOLIC FUNCTIONS IN EXPERIMENTAL ANIMALS AFTER INTRODUCTION OF THE XENOBIOTIC, IMMUNOTROPIC DRUG AND PROBIOTIC

Zvyagintseva O.V., Klimova E.M., Lavinska O.V., Lenkevich A.S.

The aim of the study was to evaluate *in vivo* changes in metabolic and barrier function of the resistance factors (activity of enzymes of neutrophils, the efficiency of phagocytosis), some biochemical parameters (concentration of ceruloplasmin and haptoglobin) and proliferative activity *in vitro* cells after introduction of copper sulfate, probiotics and immunostimulant "Fungidol" the experimental animals.

Material and methods. The *in vivo* experiments were performed on 6-month-old male rats of Wistar line. Identified the following groups: group 1 - control animals, which were intraperitoneally injected with saline (n = 5); group 2 - animals that were administered saline *per os* and 48 hours a solution of copper sulphate intraperitoneally (n = 5); group 3 - animals, which were injected with immunotropic drug "Fungidol" *per os* and 48 hours a solution of copper sulphate intraperitoneally (n = 5); group 4 animals, which were injected with a solution of probiotics *per os* and 48 hours a solution of copper sulphate intraperitoneally (n = 5). As a probiotic used capsules firm Yogurt that contains active *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus*. The concentration of haptoglobin and ceruloplasmin were determined spectrophotometrically. Oxygen-dependent metabolism of neutrophils was investigated by microscopy according to their ability to absorb nitroblue tetrazolium (NBT-test) and restore it to deformation in the form of granules blue color under the influence of superoxide anion, which is formed in the NADP-oxidase reaction, initiating the process of stimulation of phagocytosis (NBT-test). To determine the barrier function of phagocytic cells by light microscopy to evaluate the activity of phagocytosis of neutrophilic granulocytes with subsequent determination of phagocytic index, phagocytic number and the index of completeness of phagocytosis. As a microbial agent used is a suspension culture of *Saccharomyces cerevisiae*. The peripheral blood leukocytes were cultured according to the method of Hereford in medium 199 with the addition of fetal calf serum in the absence and in the presence of T-cell mitogen – phytohemagglutinin.

Results and discussion. In all studied groups (introduction of the xenobiotic, "Fungidol", probiotic experimental animals revealed a significant increase in the concentrations of ceruloplasmin and haptoglobin on the average in 1,5 times in comparison with the control, indicating the development of the inflammatory process after the toxic action of copper sulphate.

During administration of sulphate of copper, the experimental animals showed a reduction in the index of completion of phagocytosis, indicating a failure of the process of endocytosis of bacterial antigens and reduced stimulation index due to the low activity of NADP-oxidase system of phagocytes. The introduction of xenobiotic animals was increased 1,2 times compared with the control (23,33±1,38) % the number of transformed cells in the background of mitogenic inducer of cell proliferation. The proliferative activity of hemolytic after the joint action of the xenobiotic and immunotropic drug in cell culture with the mitogen was the highest and exceeded 1,5 times control (23,33±1,38)%. After the introduction of copper sulfate and probiotic proliferative activity of hemolytic was also significantly higher spontaneous.

Introduction biologic response modifier substance to a greater extent than probiotics stimulate a protective immune processes aimed at combating the negative effect of the xenobiotic.

Conclusion. Thus, the introduction of copper sulfate launches in animals a cascade of reactions aimed at the disruption of homeostasis. It is a violation of various physiological processes of digestion, respiration, cell differentiation, water-salt metabolism, metabolism of carbohydrates, proteins, lipids, detoxification of exogenous substrates and metabolites, production of biologically active compounds. Introduction immunostimulant and probiotics, in varying degrees, led to activation of protective mechanisms under the action of stress factors aimed at the adaptation and translation of the body into a new functional state.

Keywords: xenobiotic, immunotropic drug, probiotics, immune response.

АНТИВІРУСНА І АНТИМІКРОБНА АКТИВНІСТЬ РЕЧОВИН І ЛІКАРСЬКИХ ФОРМ (ANTIVIRAL AND ANTIMICROBIAL ACTIVITY OF SUBSTANCES AND DOSAGE FORMS)

THE STUDY OF THE ANTI-INFLUENZA ACTIVITY OF ALTABOR SUBSTANCE

Rybalko S.L., Krutskykh T.V., Shalamay A.S.

The antiviral activity of Altabor substance has been studied in the experiments *in vitro* and *in ovo*. The substance of Altabor actively inhibits the influenza virus reproduction in the doses from 100 µg/ml to 6,75 µg/ml by 7,5-3,0 lg of ID₅₀, drug in the dose of 100 µg/embryo inhibits the replication of the influenza virus by 5,5 lg of EID₅₀, and it confirms the presence of the antiviral activity of the drug.

Key words: altabor, antiviral activity, influenza.

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ИЗУЧЕНИЕ ПРОТИВОМИКРОБНОЙ АКТИВНОСТИ КОМБИНИРОВАННЫХ ПРЕПАРАТОВ НА ОСНОВЕ ПЕРОКСИДА ВОДОРОДА И ЭТОНИЯ

Блажеєвський Н.Е., Бойко Н.Н.

THE STUDY ANTIMICROBIAL ACTIVITY OF COMBINATION DRUGS ON THE BASIS OF HYDROGEN PEROXIDE AND AETHONIUM

Blazheyevskiy, N.Ye., Boyko, N.N.

Formulation of two complex antimicrobial compositions on the basis of hydrogen peroxide and aethonium has been developed: hydrogen peroxide – 16.7 %; aethonium – 12.0 %; sodium pyrophosphate – 0.06 %; water and stabilizing agents up to 100 % (composition 1) and hydrogen peroxide – 18.0 %; aethonium – 12.0 %; ethanol – 12,5 %; water and stabilizings agent up to 100 % (composition 2); and their antimicrobial activity has been studied by agar diffusion method on standard microorganism test strains: *Staphylococcus aureus* ATCC 25923; *Staphylococcus aureus* ATCC 6538; *Escherichia coli* ATCC 25922; *Escherichia coli* ATCC 11229; *Pseudomonas aeruginosa* ATCC 27953; *Pseudomonas aeruginosa* ATCC 15442; *Proteus vulgaris* H 4636; *Proteus mirabilis* ATCC 14153; *Enterococcus faecium* ATCC 6057; *Bacillus cereus* ATCC 10702; *Candida albicans* ATCC 10231. We have carried out assessment of integrated antimicrobial activity of complex drugs using vector algebra. It has been demonstrated that there is a direct correlation between the integrated index of antimicrobial activity and logarithm of concentration of antimicrobial components in the solution. An advanced mathematical model for description of the dependence of activity spectrum on concentration of antimicrobial drugs has been suggested – logistic dependence. It has been determined that composition 1 is 13.5 % more active when compared to composition 2. In the result of the study of antiseptic compositions 1 and 2 in the following dilutions: undiluted, 1:2, 1:4, 1:8, 1:16, and determination of their microbicidal activity associated with 1-3-5-10-30-60-minute exposition with microbial burden of clinical and test strains $2 \cdot 10^9$ CFU/mL using the method for assessment of antimicrobial activity of drugs developed, we have come to the conclusion that antimicrobial properties of the compositions studied maintain at the high level up to their dilution to 1:4; at this dilution, an optimal bactericidal exposition of 10 min has been determined. We have come to the conclusion as for potential of use of the combined antimicrobial compositions on the basis of hydrogen peroxide and quaternary ammonium compounds suggested as antiseptic agents and disinfectants in medicine and/or veterinary.

Key words: disinfection, hydrogen peroxide, aethonium, antimicrobial properties.

MORPHOLOGICAL ALTERATIONS OF *STAPHYLOCOCCUS AUREUS* CAUSED BY ARYLALIPHATIC AMINOALCOHOL DERIVATIVE

Dronova M.

Increasing of antimicrobial resistance has created a critical need of the novel antimicrobial agents. One of the promising chemical classes for its development are aryl aliphatic aminoalcohols. New compounds of this class were synthesized at the Institute of organic chemistry (Kiev, Ukraine), by Y. Korotkiy. After the screening studies compound KVM-194 was selected as the potent antistaphylococcal agent. The aim of the study was to examine ultrastructural changes in the bacterial cells under the influence of the compound KVM-194.

Materials and methods. *Staphylococcus aureus* ATCC 25923 was used in all experiments. The minimum inhibitory concentration was determined by serial macrodilution method in Mueller-Hinton broth. Bacteria were exposed to the 0,5 MIC and 5 MICs of the KVM-194 for 1 h and 24 h. Ultrastructure of intact and treated *Staphylococcus aureus* cells was examined by transmission electron microscopy after contrasting by osmium tetroxide and lead citrate.

Results and Discussion. The compound KVM-194 possesses a distinct antibacterial activity against *Staphylococcus aureus*, the minimum inhibitory concentration is 1.25 µg/ml. We found that exposure to KVM-194 at a subinhibitory concentration resulted in alterations of the cell morphology even after 1 h of treatment. The roughness of the cell surface and emerging of the intracellular particles of different electron density were observed. Increase of the incubation time to 24 h led to detachment of membrane from cytoplasm, multi-membrane structures within cells emergence and formation of nonpolar septum. 1 h exposition to suprainhibitory concentration of KVM-194 resulted in nucleoid fragmentation, septum abnormalities and necrosis of some cells. We found that increasing of the incubation period to 24 h led to exacerbation of alterations: cell wall rupture, leakage of cytoplasm and a large number of lysed cells were registered.

Conclusion. Observed alterations, suggest the possible mechanism of action of KVM-194, due to its influence on the cell membrane and intracellular processes.

Key words: *Staphylococcus aureus*, antibiotics, mechanism of action, aryl aliphatic aminoalcohols.

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ДОСЛІДЖЕННЯ ПРОТИМІКРОБНОЇ АКТИВНОСТІ НОВОЇ КОМБІНОВАНОЇ МАЗІ НА МОДЕЛІ ГНІЙНОЇ РАНИ СТАФІЛОКОКОВОЇ ЕТІОЛОГІЇ

Ткачова О. В.

STUDY OF ANTIMICROBIAL ACTIVITY OF NEW COMBINED OINTMENT ON THE MODEL OF PURULENT WOUND OF STAPHYLOCOCCAL ETIOLOGY

Tkachova O. V.

Introduction. Prevalence of purulent pathologies and insufficient number of combined ointments with multi-effect on inflammation, infection and tissue damage are a prerequisite for scientists of NUPh to develop a new combined ointment composed of: antiseptics ethacridine lactate and thick chlorophyllipt extract, drug with reparative and anti-inflammatory activity – dexpanthenol, PEG-base of the IInd generation with the moderate dehydrating activity (180%). The range of pharmacological actions of Filetol ointment meets local therapy requirements in the IInd phase of the wound healing process. New ointment can also be applied in the Ist phase of wound healing process, if the wound contains a small amount of purulent exudate or does not contain it at all.

Material & Methods. The purulent wound of staphylococcal etiology was reproduced in 24 white mature female mice weighing 14-17 g and subcutaneously injected with 0.2 ml of 10% solution of calcium chloride in the skin area, depilated beforehand, and after the development of necrosis on the 4th day injected with 0.2 ml of daily agar cultures *S. aureus* ATCC 25923 in the necrotizing area. In 48 hours of the infection, in the area of administration of staphylococcus cultures purulent necrotic wounds developed, which, depending on the size and intensity of the lesions, were subjected to reverse development in 9-15 days in a row. Animals were divided into three groups of 8 animals, including a positive control group, animals in which were not treated. In this study, the comparator was Levomecol ointment which is widely used in clinical practice for the local treatment of purulent wounds. Efficacy of treatment was evaluated on the basis of lesion value and intensity in study groups compared with the positive control, animal deaths in the case of generalization of the purulent process, quantitative dynamics of microorganisms in the wound and planimetric indicators (area of wounds and the percentage of rats with healed wounds).

Results & Discussion. Intradermal administration of staphylococcus to mice resulted in the development of severe purulent necrotic wounds in animals which in the positive control group was accompanied by increase in titer of microbial contamination during the experiment. Due to the generalization of infection, high mortality of animals was observed and in the positive control group it amounted to 50%. Application of Filetol ointment contributed to the rapid cleansing of wounds from purulent necrotic masses, reducing the number of microorganisms and activation of

reparative processes. From the 3rd day of treatment with Filetol ointment, content of *S. aureus* in the wound decreased by half and was $2 \times 10^3 - 3 \times 10^4$. Full liberation of wounds of *Staphylococcus* in the treatment with Filetol ointment was observed on the 6th day of treatment. In animals treated with Levomecol ointment, liberation of wounds of *Staphylococcus* took place 3 days later.

Conclusion. Use of Filetol ointment contributed to preventing the generalization of infection process in mice which affected the growth of the animal survival by 25% compared to the positive control and by 12.5% compared to Levomecol ointment as well as acceleration of healing of purulent wounds.

Keywords: ointment, antimicrobial, staphylococcus, wound

ИЗУЧЕНИЕ ВЛИЯНИЯ КОМБИНАЦИЙ ЦИПРОФЛОКСОЦИНА С ДРУГИМИ АНТИБИОТИКАМИ НА ПОЛИРЕЗИСТЕНТНЫЕ ШТАММЫ СИНЕГНОЙНОЙ ПАЛОЧКИ Дьяченко В.Ф. Марюшенко А.М., Ягнюк Ю.А.

THE STUDY OF ANTIMICROBIAL ACTION OF COMBINATION OF CIPROFLOKSACIN WITH ANTIBIOTICS AGAINST POLYANTIBIOTIC-RESISTANT STRAINS OF PSEUDOMONAS AERUGINOSA BY OF CHECKERBOARD METHOD

Dyachenko V.F. Mariushchenko A.M., Yagnuk Yu.A.,

Pseudomonas aeruginosa is one of the man caused of opportunistic infections. The rapid decrease in sensitivity of pathogens septic infections to antimicrobial agents has led to significant difficulties in the treatments of antibiotic-resistant infections. One solution to this problem is a method of combining antimicrobial medications of different pharmacological groups. Antimicrobial synergy resulting from antibiotic combination therapy is often important in the treatment of serious bacterial infections.

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Materials and methods. *Pseudomonas aeruginosa* strains used in this study were isolated from hospitalized patients at the Hospital of the Surgery of Kharkov. The study of combinations of antibiotics efficacy was carried out by determining the minimum inhibitory concentrations using routine method in vitro method "checkerboard". Fractional inhibitory concentration indices were calculated for all isolates with all combinations. The present paper investigates the synergic effects of ciprofloxacin in combination with tienam, amikacin or cefepim.

Results and discussion. Calculation of the FIX showed that the combination of ciprofloxacin with cefepim demonstrated synergistic inhibitory activity against 66,6 % of *Paeruginosa* strains tested. Thus studies have shown the indifferent summation effects of combinations of ciprofloxacin with tienam or with amikacin on the majority of multiresistant strains of *P.aeruginosa*.

Conclusion. The result of experimental study by of checkerboard method was shown the high effectiveness of the combinations of ciprofloxacin and cefepime in relation to *Pseudomonas aeruginosa* polyantibiotic-resistant strains

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

ВИВЧЕННЯ АНТИМІКРОБНИХ ВЛАСТИВОСТЕЙ ДЕЯКИХ ВИДІВ САПРОФІТНИХ ОБЛІГАТНИХ МОРСЬКИХ ГРИБІВ

Калюжная О. С.

STUDY OF THE ANTIMICROBIAL PROPERTIES OF CERTAIN SAPROPHYTIC OBLIGATE MARINE FUNGI

Kalyuzhnaya O. S.

Today promising area of the development and introduction of new antimicrobial agents is to search for new antibiotics from natural sources, namely among marine organisms - microscopic fungi. Such saprophytic fungi as *Ascomycota* (families *Arenariomyces*, *Ceriosporopsis*, *Corollospora*, *Halosphaeria*) and *Basidiomycota* (family *Nia*), which are widely spreaded in Ukraine (salty estuaries and the coast of the Black Sea), are the objects of the study of this work.

These types of marine organisms have been provided by the Odessa Branch of the Institute of Biology of the Southern Seas after collecting samples of water, sediment, cellulose substrates and subsequent isolation and obtain pure cultures by accumulation in the form fruiting bodies of *Ascomycetes* and *Basidiomycetes* - ascocarps and basidiocarps that can be stored 3-5 months in sterile seawater. The aim of this study was to investigate the presence of antimicrobial properties of saprophytic fungi obligate marine, which are characteristic for residents in Ukraine, namely the Black Sea.

Materials and methods. At this stage the study of antimicrobial activity was performed by agar diffusion method and method of cocultivation of marine fungi with test strains in liquid culture medium. We have used reference strains of microorganisms: *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Bacillus subtilis* ATCC 6633, *Proteus vulgaris* ATCC 6896, *Pseudomonas aeruginosa* ATCC 27853 and opportunistic fungus *Candida albicans* ATCC 885-653.

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Results and Discussion. Determination of antimicrobial activity by agar diffusion method showed that all samples had antimicrobial activity against the Gram-positive test strains (*S. aureus* and *B. subtilis*), effect for the Gram-negative bacteria (*E. coli*, *P. vulgaris*, *P. aeruginosa*) was much smaller or non-existent, and it isn't observed against *C. albicans* (exclusion *Nia vibrissa* with zone of growth inhibition – 6.2 mm). The results of the counting of cells test strains of *E. coli* and *S. aureus* in control and after their cocultivation with fungi *Halosphaeriopsis mediosetigera* and *Nia vibrissa* on yeast broth at $(37 \pm 1)^\circ \text{C}$ showed that the number of test cells after culturing strains with selected species of marine fungi significantly lower than in control: when cultured with *Halosphaeriopsis mediosetigera* cell number of *E. coli* decreased by almost 100 times, and cells of *S. aureus* - 1000, when cultured with *Nia vibrissa* number of cells test strains decreased 100 times. These results prove the presence of antimicrobial properties for these species, with observed the same trend as the study of antimicrobial properties of agar diffusion method - both types of fungi inhibit gram-positive and gram-negative bacteria.

Conclusions. The study of the antimicrobial properties of some species of saprophytic obligate marine fungi, which are the inhabitants of the north-western Black Sea region: *Arenariomyces trifurcata*, *Ceriosporopsis halima*, *Corollospora maritima*, *Halosphaeriopsis mediosetigera*, *Nia vibrissa*, was carried out. It was established that their culture supernatant have antimicrobial activity against gram-positive bacteria, and the last two species - against gram-negative bacteria, such action was not observed against *C. albicans*. Thus, the selected objects of study are potential producers of antimicrobial substances; it leads to the prospect of further work in this area.

Keywords: saprophytic obligate marine fungi, antimicrobial properties

МІКРОБІОЛОГІЯ (MICROBIOLOGY)

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF YERSINIOSES IN KHARKIV REGION

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Mohylenets O.I.

Despite great success in diagnostics of infectious diseases and development of new laboratory methods, vast majority of cases are not diagnosed or registered as different diagnosis. It connected with polymorphism of clinical signs and difficulty of specific diagnostics. The most evidential method of diagnostics is culture, but grows of *Yersinia spp.* on common media is very bad. More specific and modern methods are immunofluorescence analysis (IFA), polymerase chain reaction, immunoblot analysis, but this methods are rather expensive and require specialized laboratory equipment and staff. Indirect hemagglutination test (IHAT) is still more common in Ukraine.

Materials and methods The object of the study were 61 patients with yersiniosis who were treated in the Kharkiv Regional Clinical Infectious Diseases Hospital during five years. The diagnosis of yersiniosis in all patients was based on epidemiological, clinical, anamnestic data; results of additional laboratory studies which were in accordance with generally accepted clinical criteria. Final diagnosis was confirmed by results of serological studies (IHAT in pair serum with *Yersinia enterocolitica* 03, *Yersinia enterocolitica* 09 and *Yersinia pseudotuberculosis* antigen). For exclusion of viral hepatitis patients with jaundice were checked for anti-HAV IgM, HbsAg, and anti-HCV IgG by IFA.

Statistical data processing was carried out by means of Statistica 6.0 software package. Comparative group analysis was performed by using χ^2 (Pearson) criterium. Differences with $p < 0,05$ were considered statistically significant.

Results and Discussion From the 61 patients that were under our supervision, in 59 was diagnosed intestinal yersiniosis, in 2 – pseudotuberculosis. Patients up to 50 years old were dominated. The incidence was recorded throughout the year in the form of sporadic cases. The severity of the disease in most cases was moderate (55,7%) or mild (32,8%). Severe disease was registered in 7 patients. Generalized (46%) and gastrointestinal (42%) forms dominated. Most patients – 39 (64%) – experienced acute onset of the disease. Climax period was characterized by considerable polymorphism. Intoxication syndrome was predominant. Catarrhal, gastrointestinal and abdominal syndromes, hepatomegaly, polylymphadenopathy and rash were observed often enough. Arthralgic syndrome, splenomegaly, kidney affection were revealed less frequently.

Conclusions 1. In the Kharkiv region intestinal yersiniosis prevailed above pseudotuberculosis. The main causative agent is *Y. enterocolitica* O3. 2. Disease was registered as sporadic cases, that occurred throughout the year. Male persons of working age were mainly affected.

3. The clinic of yersiniosis was characterized by pronounced polymorphism, which lead to difficulties in diagnosis. About half of patients had signs of process generalization. 4. Specific laboratory methods, including IFA and PCR (as addition to stool culture and IHAT), should be prescribed to reveal real situation about incidence of disease, improve the diagnostics and further treatment.

Key words: yersiniosis, clinical, epidemiological data

THE ASPECTS OF INVESTIGATION OF MICROORGANISM ANTIBIOTIC RESISTANCE AT THE PRESENT STAGE

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Introduction. At the present stage for ensuring epidemic safety and prevention of nosocomial infections the complex of analytical study and managerial procedure to improve the epidemiological supervision over nosocomial infections through the introduction of infection control in health care practice are using. The microbiological monitoring is part of the infectious control and allows supervising circulation of microorganisms and their antimicrobial resistance by dynamic observation over structure and level of resistance to antibiotics that are used in the given particular hospital.

Materials and methods. For the dynamic observation of the structure and the level of resistance of microorganisms to antimicrobial agents the computer software WHONET recommended by WHO has been used. With using WHONET in Dnepropetrovsk Children's Hospital № 3 the computer database has been created. In this database the information about each patient, hospital department, samples under test and the date of its excretion, the data about the detected microorganism and its sensitivity/resistance to antimicrobial agents have been stored. The examination and analysis of antibiotic resistance of microorganisms has been provided for 2010-2014 years, in total the data on 6168 isolates from 3876 patients have been analyzed.

Results and discussion. By the total data the isolates belong to a wide spectrum of microorganisms (more than 40 different types). By means of the analysis of isolating of clinically significant microorganisms it has been established that one of the most frequent isolated were *Escherichia coli* (1-20 %), *Klebsiella pneumoniae* (4-18 %), *Staphylococcus epidermidis* (1-12 %), *S. aureus* (1-10 %), *Enterobacter cloacae* (2-9 %), *Pseudomonas aeruginosa* (1-8 %). Detection of other microorganisms was irregular and its frequency is varied from 0 % to 10 %. As a result of examining the sensitivity of microorganisms it has been shown that tested strains of bacteria were resistant to 72.7 % (on the average) of antibiotics used in testing. In particular, resistance to ampicillin, ceftriaxonum, ceftazidime and gentamycin was high and reached 100 %. After the placed ban on the usage of these medicines in dynamics, there was observed a tendency to development to ampicillin, ceftriaxonum, ceftazidime and gentamycin in circulating strains of microorganisms.

Conclusion. Improving quality of medical aid is possible by implementation of strategy of controllable application of antibiotics based on the results of microbiological monitoring using analytical computer program WHONET in practice of health protection establishments.

Keywords: antibiotic resistance, microbial monitoring, WHONET.

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ПІДХІД ДО СПЕЦИФІЧНОЇ ДІАГНОСТИКИ ЗБУДНИКІВ ІНФЕКЦІЙНОГО ЕНДОКАРДИТУ

Кацапов Д.В.

APPROACH TO SPECIFIC DIAGNOSTICS OF CAUSATIVE AGENTS OF INFECTIOUS ENDOCARDITIS

Katsapov D.V.

Introduction. Increased level of morbidity of infective endocarditis (IE) connected with new risk factors: intravenous drug use, cardiosurgical interventions, hemodialysis brought new clinical forms of the disease. As it shown in a literature main pathogenetic factors of IE are bacteraemia, trauma of endocardium and invasive medical procedures. Very typical pathogens are streptococci and staphylococci. Most typically mitral and aortal valves are affected with spreading of vegetations on surrounding media.

Discussion. IE is polyetiologic disease caused by more than 128 microorganisms, and still a challenge for medical professionals. Detection a causative agent is critical for proper specific treatment. In different sources data on percentage of proven cases very according to country and different medical centres reflecting different local epidemiology of IE, diagnostic criteria and protocols.

Culture negative infectious endocarditis (CNIE) is considered in case of obtaining of three negative results of cultivation of samples on a standard blood agar during 7 days and subculturing. CNIE incidence very form 2% to 33% according to different researches and higher in cases of community acquired infection and reseeded antibacterial treatment. Some of cases of CNIE caused by gram - negative fastidious microorganisms - *Haemophilus parainfluenzae*, *Actinobacillus*, *Actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*, with united in HACEK group according to their properties to colonize oropharynx and requirement in special conditions and duration of incubation. Detection of some intracellular bacteria, such as *C. burnetti* and *Bartonella spp.* require immunological methods of detection, histological methods and of PCR.

Conclusion. In case of diagnostics of patients with CNIE it is necessary to use a combination of prolonged subculturing of serum, emboli and histologic material on blood agar with microscopy by Warthin-Starry, Gimenez and PAS with serologic methods and broad - range PCR amplification.

Keywords: infectious endocarditis, *Haemophilus parainfluenzae*, *Actinobacillus*, *Actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*

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ЕПІЗООТОЛОГО-ЕПІДЕМІОЛОГІЧНІ ОСОБЛИВОСТІ ЛЕПТОСПИРОЗУ В

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ТЕРНОПІЛЬСЬКІЙ ОБЛАСТІ

Кравчук Ю. А., Васильєва Н. А.

EPIZOOTIC AND EPIDEMIOLOGY FEATURES FOR LEPTOSPIROSIS IN TERNOPIL REGION

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Introduction. Leptospirosis is the most widespread zoonotic diseases in the whole world. In Ukraine leptospirosis is registered practically in all regions, however very much unevenly, that it is related to the level of acidity of soils. One of such regions there is the Ternopil region.

Materials and methods. Were based on official statistics of the incidence leptospirosis in the Ukraine regions and carried out anti-epidemic activities in 1984-2014.

Results & discussion. Ternopil region was expressed of leptospirosis with epizootic and epidemic level. The level of morbidity of people in this region exceeded middle state index and hesitated within the limits of 1,05-12,17 on a 100 thousand population, the most getting up was on 1992-2001 for of the last 30 years. The level of morbidity is increase at the end of summer and in autumn (at most in September), that, probably, it is related to the increase of quantity of rodents and "bathing" season. The etiologic structure of leptospirosis in region was by *L. rippotyphosa* at 1981, in 90th – *L. icterohaemorrhagiae*, later were *L. hebdomadis*, *canicola* and *pomona*, first – *L. kabura* and *L. polonica*, at the same time part of *L. icterohaemorrhagiae* grew short to 37,5 %, diseases, caused *L. grippotyphosa*, – rare and not annually. In 2010 diseases were predefined by *L. icterohaemorrhagiae* and *L. canicola*, in 2011 – *L. canicola*, *L. icterohaemorrhagiae*, *L. pomona*. In 2012 from 19 cases of 10 were caused by *L. canicola*, in 2013 from 26 – 12, in 2014 from 35 – 7. From 2004, became more frequent the mixed leptospirosis, part of which in separate years arrived at 25-37 % among. The agricultural animals (cattle, pigs, horse) and dogs are the independent reservoir of leptospirosis. The agricultural animals and possibility of transmission by alimentary way of causative agent were assist maintenance of continuous epizootic process an circulations of causative agent in an interepidemic period during great while without the receipt of leptospirosis from a natural reservoir. Was present the direct correlation between temperature of air and level of morbidity of people ($r=0,77$) and the same between the amount of precipitations and level of morbidity ($r=0,79$).

Conclusion. The abiotic (climatic-ground terms, temperature of air, amount of precipitations) and biotic factors (vegetation, quantity and infected of rodents, and also other warm-blooded owners) of were confirmed as natural reservoir of leptospirosis. The difference of soils acidity makes territorial division of disease, because leptospirosis is survive in alkaline soils and die quickly in acid.

Keywords: leptospirosis, morbidity, Ternopil region.

ПОРІВНЯЛЬНА ЦИТОЛОГІЧНА ДІАГНОСТИКА МАЗКІВ КРОВІ ПРИ БАБЕЗІЙНІЙ ІНФЕКЦІЇ

Похил С.І., Торяник І.І., Тимченко О.М., Чигиринська Н.А., Костира І.А.

COMPARABLE CYTOLOGICAL DIAGNOSTIC OF BLOOD SMEARS ON BABESIA INFECTION

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In last time Babesiosis as a tick-borne hemoprotozoans human disease have a very important role in differential diagnostics of modern infectious medicine. It caused by protozoan of the genus *Babesia*, which invade and destroy erythrocytes. Babesiosis also has been called tick fever. So, *Babesia* has been known by other genus names, including *Nuttallia*, *Microbabesia*, *Babesiella*, and *Gonderia*. Because all *Babesia* species are piroplasmids, a more inclusive term for anthroprotozoan infections caused by these organisms would be piroplasmidosis. Their detective complicacy are build that, tick-borne disease agents from prolongate life cycles involving arthropod and vertebrate host. The complexity is enhanced by the diversity of hosts in different biotopes, which depends on factors life type of vegetation, climate and/or human influence, such as restoration of former industrial sites, which leads to the development of new biotopes. So, on the one hand, new habitats for plants and animals including ticks, and nature are created. About the first case of babesiosis infection was reported as a cause of human sickness in 1969 in northeastern United State. Several hundred cases are now reported from this region each year. The disease is characterized by a gradual onset of malaise with anorexia, fever, headaches, myalgia, and other vague symptoms, which may persist for long period. Occasionally dangerous fulminating infections occur particularly in immunocompromised or aged individuals.

The purpose of the present research was to study of the cytological diagnostic of blood smears from object's with the Babesia infection.

Materials and methods. Blood smears (by Romanovsky-Gimze (standart), Wright's standart and staining, the author's modification, 2014) of domestic dogs (n = 31) of both sexes with Babesia infection at the age from 3 months to 6 years served as the material for the study. The preparations were fixed during 1-2 seconds with 96 % ethyl alcohol. Then warmed ($t = 36.0 \pm 2.0$)°C commercial matrix solutions of eosin, azure and methylene blue were applied one by one. The smears were rinsed (1-2 seconds) in distilled water and dehydrated. The procedure ended with short-term drying in a diffused stream of warm dry air (Samsung house fan, power 220 W). The results were compared with intact control. Smears were contrasted and analysed under a microscope LOMU (LOMO, Russia): x 300; x400; x1000; x1350 and photographed with a digital camera "Canon EOS-3000".

Results. Blood samples infected with Babesia species were collected (may-october) from naturally (promenade in forest-park) tick-borne infected dogs (*Canis familiaris*) in all Kharkov region and city. All (experimental) animals were monitored twice daily by veterinary doctors for clinical signs and had rectal temperatures taken (authors have a great thankness for the cooperation and consolidation Chif -Mr. Yu. V. Al'okhin and veterinary personal of Kharkov Center of Clinical Veterinary). Blood was drawn daily for hematocrit determination and peripheral blood smear were made from ear vein blood to determine parasitemia status. As result of the analysis of blood smears it was found out that against a background of orange erythrocyte cytoplasm the preparation area easily revealed crimson- and red-lilac pyriform (n = 8-12 in the field of vision of the preparation), annular (n = 9-16 in the field of vision), amoebiform haemoparasites and those with other shapes ($\Sigma=13$), thereby indicating a high level of infection (81.8 %). Owing to their own chromatophilic feature, protozoan cells looked geometrically marked and clearly contrasted against a background of the saturated red-violet colour of nuclei. The developed technique of staining facilitated: a more qualitative analysis of ontogenetic staging (III) of Babesia (trophozoites, merozoites, sporozoites); improvement of differential diagnosis of the haemoparasites with blood platelets (the latter were distinguished from cells of the causative agent by the presence of marked ovaloid azurophilic granules in the cytoplasm of young forms ($\Sigma = 1-3$ in the field of vision) and azurophilic granularity in mature forms; better differential diagnosis with intracellular inclusions (intraerythrocytic Cabot rings, Howell-Jolly bodies); improved differential diagnosis with solid elements of sediments of used stains (the above artifacts were in a saturated dark blue or black colour and observed very seldom).

Conclusions. By the results of the cytological diagnostic of blood smears it was revealed that domestic dogs with clinically detected Babesia infection had a high level of contamination with parasites. In our studies this level was 81.8 %. Has been established that using of the blood smears by Romanovsky-Gimze in Wright's the author's modification (2014) are very effective to extrimal medicine and perspective for next clinical investigation.

Keywords: babesia infections, cytology, diagnostics

H. PYLORI ТА ГАСТРОПАТІЯ ПРИ ЦУКРОВОМУ ДІАБЕТІ

Коваль В.Ю.

H. PYLORI AND GASTROPATHY IN DIABETES

Koval V. Yu.

Over the last 11 years the prevalence of diabetes in Ukraine has increased rapidly – from 1.8 to 2.8%. This especially concerns children and adolescents. The progression and compensation of the diabetes depend on many factors. In today's medical literature the role of *Helicobacter pylori* in the development and progression of diabetic gastroparesis is widely discussed. In addition, the issue of the necessity and feasibility of *H. Pylori* eradication in these patients is also keenly discussed. The results are rather contradictory. The results of infection of *H. pylori*, the peculiarities of progression, the impact on the compensation of *H. pylori* in patients with diabetes of I and II type are provided in this article.

Materials and methods. The study included 52 patients with diabetes in which the erythematous and erosive gastropathy were found during fibrogastroduodenoscopy. The diagnosis of diabetes was set according to the criteria of the American Diabetes Association, year 2010. The patients were treated at the gastroenterology and endocrinology department of the A. Novak Uzhhorod Regional Clinical Hospital. Glycated hemoglobin (HbA1c) was measured in all of the patients. *H. pylori* was measured by a quick test for determining the *Helicobacter pylori* antigen in the stool using the test system Cer Test Diotec Sl., Spain.

Results and discussion. 65% of the women and 35% of the men were studied. The group with type I diabetes comprised of 76% women and 24% men, and with type II diabetes – 44% women and 56% men. The age of the patients with type I diabetes – 44.5±3.79 years, type II diabetes - 51±3.86. The study of the patients with type I diabetes has shown the presence of *Helicobacter* infection in 35% of the patients. In patients with type II diabetes the presence of *H. pylori* antigen in stool was found in 77% of the patients. In patients with type I diabetes infected with *H. pylori* (first group) asthenoneurotic syndrome prevailed in the clinical progression: general weakness in 83% of the infected with *H. pylori*, and in 91% *H. pylori* in not infected patients with type I diabetes. Weight loss was registered in 67% of the first group and in 36% of the second group, dyspeptic syndrome: nausea in 71% (not infected – 50%), vomiting – 43% (25%), heartburn – 57% (0%), constipation – 43% (50%), diarrhea – 21% (25%). Dry mouth was registered in 67% of the patients with type I diabetes infected with *H. pylori*, and in 91% of not infected. Polydipsia was registered correspondingly: in 52% of the patients from group I, and in 82% of the patients from group II. In patients with type II diabetes infected with *H. pylori* (third group) the dyspeptic syndrome prevailed in the clinical progression: nausea in 78% (not infected – 50%). Vomiting – 57% (21%), heartburn – 71% (25%), constipation – 43% (50%), diarrhea – 28% (25%). Dry mouth was registered in 71% of the patients with type II diabetes infected with *H. pylori*, and in 100% of not infected with *H. pylori* (fourth group). Polydipsia was registered correspondingly in 50% of the patients from the third group and in 75% of the patients from the fourth group. During the treatment the compensation of type I diabetes infected with *H. pylori* was registered in 42% of the patients, and not infected with *H. pylori* – 84% of the patients before the end of the first week of treatment. In type II diabetes with *Helicobacteriosis* the compensation of the diabetes occurred in 29% of the patients before the end of the week. In patients with type II diabetes without *Helicobacteriosis* the compensation was registered in 75% of the patients.

Conclusions. 1. *Helicobacteriosis* was registered in 35% of the patients with type I diabetes, and in 77% of the patients with type II diabetes. 2. In patients with type I and type II diabetes infected with *H. pylori* nausea, heartburn, vomiting, general weakness and weight loss are observed more often in the clinical progression. 3. The presence of the *Helicobacter* infection in patients with type I and type II diabetes has a negative effect of the terms of diabetes compensation on the background of treatment. 4. Taking into account the relatively high incidence of *Helicobacter* infection in patients with diabetes it is necessary to include the determination of the *H. pylori* infection for differential diagnostics with diabetic gastropathy.

Key words: *H. pylori*, diabetes, erythematous and erosive gastropathy.

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ОЦІНКА ЕФЕКТИВНОСТІ ЗАСТОСУВАННЯ ДЕКАСАНУ, ДЕКАМЕТОКСИНУ ТА ЙОГО КОМПОЗИЦІЇ У ПАЦІЄНТІВ З ВАЖКОЮ ТЕРМІЧНОЮ ТРАВМОЮ

Назарчук О.А., Нагайчук В. І.

ESTIMATION OF THE EFFECTIVENESS OF DECCASAN, DECAMETHOXIN AND ITS COMPOSITION USAGE IN PATIENTS WITH SEVERE THERMAL INJURY

Nazarchuk O. A., Nagajchuk V. I.

Introduction. Nowadays victims with burn trauma are one of the most important categories of patients in the emergent surgery. According to the data of WHO burns happen in 5,6 – 10 % of cases among all kinds of trauma. Purulent-inflammatory complications in these patients are of great importance. The aim was to study microbiological, clinical effectiveness of antiseptics, antimicrobial composition of decamethoxin with modified polysaccharides, antimicrobial materials in prophylaxis and treatment of infectious complications in patients with burn injury.

Materials and methods. In the research microbiological study of antimicrobial activity of modern antiseptics, antimicrobial materials against opportunistic pathogens of purulent-inflammatory complications in patients with difficult burn injury and clinical observation of effectiveness of the use of antimicrobial composition (AMC) of decamethoxin (DKM) with carboxymethylamylum, oxyethylcellulose, polyvinylacetate. There were 130 patient with difficult burn injury (the 3rd- 4th stages; injury square – 10,0 – 85,0 % of surface) enrolled in the study. All patients underwent early surgery on the 2nd-3rd day after trauma. Complex intensive care was provided to every patient. Microbiological examinations of patients (100 %) were carried out before antibacterial treatment and every 7 days during treatment. Antimicrobial qualities of antiseptics (deccasan, miramistin, chlorhexidine digluconate) and AMC against *S. aureus* (n 35), *S. epidermidis* (n 12), *Enterococcus spp.* (n 9), *P. aeruginosa* (n 39), *A. baumannii* (n 54), *Proteus spp.* (n 16), *Enterobacter spp.* (n 11), *K. pneumoniae* (n 12), *E. coli* (n 9), *C. albicans* (n 7) were studied according to standard methods. Antimicrobial qualities of dressings, containing antiseptics we studied on clinical strains of *S. aureus*, *E. coli*, *P. aeruginosa* on dense medium, counting diameter of growth delay zones (mm).

Results and discussion. Results of study of sensitivity of Gram-positive and Gram-negative pathogens of purulent-inflammatory complications in patients with severe thermal injury to antiseptics (deccasan, miramistin, chlorhexidine) and antimicrobial composition of decamethoxin (AMC) presented advantages of antimicrobial activity of deccasan, AMC against *S. aureus*, *S. epidermidis*, *Enterococcus spp.*, *P. aeruginosa*, *A. baumannii*, *Proteus spp.*, *Enterobacter spp.*, *K. pneumoniae*, *E. coli*, *C. albicans* in comparison with miramistin (<0,001), chlorhexidine digluconate (<0,001). Antimicrobial qualities of antimicrobial gauze, impregnated with AMC, against *S. aureus* (32,4±0,5 mm), *E. coli* (26,4±0,3 mm), *P. aeruginosa* (20,8±0,34 mm) were higher than in textile materials containing chlorhexidine. Clinical effectiveness of the use of materials, impregnated with AMC, for prophylaxis and treatment of purulent-inflammatory complications in patients with severe thermal injury was proved. Microbial load of *P. aeruginosa* in wounds, where gauze with AMC was used, decreased from 7,1 x 10⁷ CFU/ml (before treatment) to 2,9 x 10⁵ CFU/ml (7th day). In control group *P. aeruginosa* colonized wounds 1 x 10⁸ CFU/ml (before treatment), and 3,2 x 10⁷ CFU/ml (7th day). The same tendency was found for *A. baumannii*.

Conclusions. Modern antiseptics deccasan and AMC have high antimicrobial qualities against Gram-positive (*S. aureus*, *S. epidermidis*, *Enterococcus spp.*), Gram-negative (*P. aeruginosa*, *A. baumannii*, *Proteus spp.*, *E. coli*, *K. pneumoniae*) bacteria and *C. albicans* which cause purulent-inflammatory complications in patients with difficult burn injury. AMC of decamethoxin demonstrate higher

antimicrobial effect against *S. aureus*, *A. baumannii*, *P. aeruginosa*, *Proteus spp.*, *E. coli* in comparison with miramistin, chlorhexidine digluconate ($p < 0.001$). AMC using for impregnation of gauze and its use in patients with burns provide high clinical effectiveness in wound infection prophylaxis.

Key words: antiseptics, decasan, decamethoxin, antimicrobial composition, burns.

ЧУТЛИВІСТЬ ДО АНТИБІОТИКІВ, АНТИСЕПТИКІВ НОЗОКОМІАЛЬНИХ ШТАМІВ *Pseudomonas aeruginosa*, ВИДІЛЕНИХ В УРОЛОГІЧНИХ ХВОРИХ

Римша О. В.

SENSITIVITY TO ANTIBIOTICS, ANTISEPTICAL NOSOCOMIAL *PSEUDOMONAS AERUGINOSA*, ISOLATED IN UROLOGICAL PATIENTS

Rymsha E. V.

Introduction. Given the active introduction into clinical practice of new groups of antibiotics and antiseptics, the problem of treatment of purulent-inflammatory complications after prostatectomy and today is relevant. Of particular concern belated cases of diagnosis and treatment of postoperative complications in urological practice patients receiving antibiotic therapy

The use of traditional antibiotics is not prevents the development of infection, because the problem of resistance of microorganisms to antibiotics and antiseptics remains relevant. The solution to the problem of development of infectious complications and prevent the formation of resistant clinical strains largely depends on the isolated pathogen, susceptibility to antimicrobial agents based on its bioavailability, ability to spread and penetrate into cells and tissues, selection of dose, interval, and route of administration to maintain minimum bactericidal concentration

Material and methods. The study involved 145 patients who were treated in the urology Department of the Vinnytsia regional clinical hospital named of M. I. Pirogov. Patients underwent the surgical treatment of benign hypertrophic prostate. Material for bacteriological studies of purulent-inflammatory diseases were urine, pieces of the prostate, remote operationally, urinary catheters, through which conducted irrigation of the bladder. Specimen collection, transportation was carried out in accordance with modern requirements. Identification was done by morphological, cultural and biochemical properties. The definition of antibiotic resistance were performed according to "guidelines for the definition of sensitivity of microorganisms to antibiotics by the method of diffusion in agar using discs" (No. 2675-83, Kiev, 2007) 12 .]. Evaluation of the results of determining the sensitivity of microorganisms to antibiotics was carried out on the basis of the determination of the zone of growth (mm) of the studied cultures around the disks with antibiotics.

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To explore sensitivity to antiseptics used commercial samples drug Decesan® (decamethoxin) of 0.02% solution ("YURI-PHARM", Ukraine), Miramistin® 0.01% solution (benzylidimethyl-myristoylation-Propylamine chloride monohydrate) (ZAO Pharmaceutical firm "Darmitsa") and Chlorhexidine (chlorhexidine digluconate) 0.05% solution (PJSC "Monfarm"). Comparative evaluation of sensitivity of microorganisms to the test preparations was determined by the minimum bactericidal concentration (MBC) standard method, serial dilutions of the drug in a liquid medium ($\mu\text{g/ml}$).

Results and discussion. Just received 20 nosocomially strains of *P. aeruginosa*. Isolated strains had the typical morphology polymorphic thin sticks, gram-negative on dense nutrient media formed a rounded, translucent colonies with a smooth edge, with a blue-green pigment. The biochemical properties referenceusa gram-negative bacteria were determined using Neverlast-24 (PLIVA – Lachema a. s. Brno, Czech Republic). The results of the determination of antibiotics susceptibility of tested strains *P. aeruginosa*. The greatest activity against the studied strains of *P. aeruginosa* had Meropenem, amikacin, ceftazidime and imipenem. Nimensa frequency of resistant strains identified to Meropenem were insensitive to 10% of strains of *P. aeruginosa*. From resistant to Meropenem 6 strains had perekhresne resistance to imipenem. The second activity with β -lactam antibiotics were identified ceftazidime. Insensitive to it were 5%. Antoniniani penicillins were less active than the carbapenems and ceftazidime. So resistant to Pirillo/tazobactam were 30% of the isolates. The most frequent combinations of stability were gentamicin – piperacillin 55,3%, gentamicin – piperacillin – piperacillin/tazobactam 35%. One strain of *P. aeruginosa* possessed simultaneously resistant to all antibiotics. Decesan and Miramistin had the same sensitivity *P. aeruginosa* ($62.5 \pm 8.94 \mu\text{g/ml}$ and $62.5 \pm 16.04 \mu\text{g/ml}$) For chlorhexidine MBC $125 \pm 8.88 \mu\text{g/ml}$.

Conclusion. Resistance nosocomial strains of *P. aeruginosa* at the present time is a serious clinical problem. Of all the antibiotics, the lowest level of resistance was determined to Meropenem. Antibacterial drugs, active against *P. aeruginosa* - Meropenem > amikacin > ceftazidime > imipenem > ciprofloxacin > piperacillin/tazobactam > piperacillin > gentamicin. Found that antibiotic-resistant strains of the *Pseudomonas* had a low level of sensitivity to antiseptics.

Keywords: *P. aeruginosa*, resistance urological patients,

НОРМАЛЬНА МІКРОФЛОРА НОСОГЛОТКИ ЯК РЕЗЕРВУАР ПОЛІРЕЗИСТЕНТНИХ ШТАМІВ ЗБУДНИКІВ ІНФЕКЦІЙ ВЕРХНІХ ДИХАЛЬНИХ ШЛЯХІВ

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Мінухін В.В., Коваленко Н.І., Ткаченко В.Л., Замазій Т.М., Самусенко С.О., Немчинович Н.Д., Шибасєва І.Б.

NORMAL NASOPHARYNGEAL MICROFLORA AS A RESERVOIR OF MULTIRESTANT STRAINS OF UPPER RESPIRATORY TRACT INFECTIONS

Minukhin V.V., Kovalenko N.I., Tkachenko V.L., Zamazii T.M., Samusenko S.A., Nemchinovich N.D., Shibaeva I.B.

Nasopharinheal carriage of bacteria may play a central role in the development and spread of respiratory infections. In addition, so-called "healthy" carriage is often transformed under the influence of various factors into an active infection. It is necessary to take into account not only the range of possible pathogens, but also trends in the development of antibiotic resistance of leading etiologic agents while choosing tactics of antimicrobial therapy. The investigation was designed to study the role of normal microflora of the nasopharynx as a reservoir of resistant strains of respiratory infections.

Materials and Methods. Fifty three healthy individuals and 168 patients with acute upper respiratory tract infections who had been treated in CEHC "Kharkiv Municipal Clinical Hospital № 30" were examined. Microbiological study included isolation and identification of pathogens in accordance with the Order of the Ministry of Health Care № 535 from 22.04.1985., determination of the sensitivity of microorganisms to antibiotics by diffusion method according to the Order of the Ministry of Health Care of Ukraine № 167 from 05.04.2007.

Results and discussion. Bacteriological study of nasal swabs of healthy people showed that the composition of the microflora of the nasopharynx contained potentially pathogenic microorganisms. Among the isolated microorganisms essential place was occupied by *S. epidermidis* and *S. aureus*, both in monoculture and association. Epidermal staphylococcus was isolated in 36 % and *Staphylococcus aureus* in 27% of cases. *Pneumococcus* and hemolytic streptococcus of group A were isolated in 23 and 14% of cases, respectively. One hundred and eighty strains of opportunistic microorganisms were isolated in the study of nasopharyngeal microflora of patients with acute upper respiratory tract infection. The leading role belonged to *S. pyogenes* (40.5%) and *S. epidermidis* (33,3%). *S. aureus* (12,8%) and *S. pneumoniae* (10,6%) were next according to. The share of *K. pneumoniae* was within 2.8%. Research of sensitivity of selected strains to antibiotics in vitro showed correlation of indices between microorganisms isolated from the nasopharynx of healthy people and

patients with acute respiratory infection. Thus, sensitivity to amoxicillin *S. epidermidis*, *S. pneumoniae* and *S. pyogenes*, isolated from the nasopharynx of healthy people was 81,8-84,2%, while low sensitivity to this antibiotic (66,7-83,6 % of isolated strains) was found for these microorganisms isolated from ill people. A similar trend was observed for isolated staphylococci and streptococci to clindamycin, doxycycline and ceftazidime. And on the contrary, the high activity of fluoroquinolones, chloramphenicol and ceftriaxone was observed for all microorganisms. I.e., the carriage in the nasopharynx of opportunistic pathogens with acquired antibiotic resistance is an important factor in the development of acute respiratory infections.

Conclusion. 1. Facultative anaerobic microflora of nasopharynx of healthy people and patients with acute upper respiratory tract infections include opportunistic microorganisms, such as *S. epidermidis*, *S. aureus*, *S. pneumoniae* and *S. pyogenes*. 2. Bacteria, isolated from the nasopharynx of healthy people and patients with acute upper respiratory tract infections, are characterized by high levels of resistance to antibiotics of therapeutic purposes. There is a correlation between antibiotic-resistant strains circulating in a healthy population and sensitivity to antibiotics of pathogens of acute respiratory infections. 3. Levofloxacin, ciprofloxacin, ofloxacin, ceftriaxone, chloramphenicol may be used as drugs of choice for the treatment of acute upper respiratory tract infections.

Keywords: nasopharyngeal microflora, antibiotics, respiratory tract infections.

ХАРАКТЕРИСТИКА АДГЕЗИВНИХ ВЛАСТИВОСТЕЙ ЛАКТОБАЦИЛ -КЛІНІЧНИХ ІЗОЛЯТІВ ТА СКЛАДНИКІВ БІОПРЕПАРАТІВ

Лаврик Г.С.

CHARACTERISTICS OF ADHESIVE PROPERTIES OF LACTOBACILLUS - CLINICAL ISOLATES AND COMPONENTS OF BIOLOGICAL PRODUCTS

Lavryk G.

Lactobacilli detected in all biotopes of digestive tract, starting from the mouth and ending with the colon, is the dominant flora of vaginal biotope. Their adhesiveness to epithelial cells leads to survive in conditions of microorganism biotopes and to form biofilm, thus mediating passive antagonism against conditionally pathogenic bacteria. Colonization resistance provides a set of mechanisms that provide individual anatomical stability and normal microflora. It is experimentally confirmed that lactobacilli provide biotopes colonization resistance of the human body due to competitive inhibition and coaggregation of allochthonous microorganisms. It is important to consider the fact that probiotics should not compete with autochthonous microflora, which is always more physiological for each individual than most valuable exogenous bacteria, even with the greatest potential beneficial properties. The probiotic activity should be directed to the main target bacterial therapy, which is to restore physiological ecological community. The aim of research was to compare the adhesive properties of lactobacilli - clinical isolates of probiotic preparations and ingredients to the buccal epithelium cells and erythrocytes 0 (1) of the blood group system AB0 person.

Materials and methods. The object of the research were clinical strains of *Lactobacillus* spp. selected from the mouth, intestines, vagina healthy people. At the the species identification of lactic acid bacteria were taken into account morphological and cultural properties, aerotolerance. The carbohydrate profile was determined using the test system API-50SN L (Bio-Merieux), lack of catalase activity. The ability of allocated bacteria to adhesion were observed in erythrocytes 0 (1) blood and buccal epithelium cells by human Brilis VI and oth. For comparison were used probiotic strains *L. rlantarum* 8P-A3, *L. acidophilus* KS 400, *Lactobacillus reuteri* DSM 17938. The effectiveness of adhesion was assessed by index microorganism adhesion (I) - the average number of microorganism on one epithelial cells that is involved in the adhesion - determined by the formula = IAM (SPA × 100) / K. We determined this rate when calculating under the microscope 50 buccal cells/erythrocytes.

Results and discussion. We received 102 strains of lactobacilli including 32 oral, 41 intestinal and 29 vaginal isolates. In species composition among isolates from all biotopes were dominated such *Lactobacillus* species: *L. acidophilus* (15 strains from the mouth, intestine - 12, vaginal - 9), respectively *L. plantarum* (4, 6, 3), *L. fermentum* (5, 10, 8), *L. rhamnosus* (4, 3, 6), *L. casei* (4, 7, 3). The only type *L. brevis* (3) just stood out from the intestine. During the research it was found that indicators of lactobacilli adhesion to buccal epithelium cells and erythrocytes 0 (1) blood are different between each other. Almost all of lactobacilli isolates showed high activity and high adhesive on the buccal epithelium. Highly adhesive appeared to be vaginal lactobacilli isolates 4,19±0,06. Among intestinal isolates the most pronounced adhesion to buccal epithelial showed *L. casei* 4,66±0,04, *L. acidophilus* 4,13±0,08. In isolated mouths of *L. acidophilus* and *L. plantarum* adhesive activity almost identical (4,12±0,07 and 4,10±0,08). It should be noted that the level of adhesion of lactobacilli to red blood cells is much lower than the buccal epithelium. Thus, the adhesion index of *L. acidophilus*, which were isolated from different biotopes to the buccal epithelium was 4,15±0,03, and - according to erythrocytes 2,50±0,01 (p>0,05). Almost all strains isolated from the intestines and vagina showed high adhesiveness to erythrocyte 2 ± 0,03 and 2,14 ± 0,02 accordingly; except *L. casei* of intestinal origin and *L. plantarum*, isolated from the vagina, which amounted IAM 3 ± 0,03 and 2,53 ± 0,08. In probiotic strains of *Lactobacillus* was observed a similar situation, but with a less expressed difference in the adhesion index on buccal epithelium and erythrocytes. The greatest adhesion observed in *L. reuteri* DSM 17 938 5,18± 0,03.

Conclusion 1. There were isolated from different biotopes of the human body 5 dominant species of lactobacilli: *L. acidophilus*, *L. fermentum*, *L. casei*, *L. plantarum*, *L. rhamnosus*. *L. brevis* was only distinguished from the intestine. 2. High adhesiveness was observed for strain *L. casei*, *L. plantarum*, isolated, both from the mouth and from the vagina, indicating a high affinity of shell structures specified types of lactobacilli in the appropriate structures of buccal epithelium. The highest adhesion to isolates from the digestive tract to found types *L. casei*. Received direct correlative relationship between an index of adhesion on buccal epithelium and erythrocytes. These data confirm that the adhesiveness is more strain feature than species. 3. In the absence of clinical manifestations of dysbiotic changes (especially in infants) to limit the use of probiotic preparations "prophylactically" as high adhesive probiotic strains may displace or inhibit the formation of its own microflora. 4. It is an open question of the effectiveness of some bio therapeutic drugs, the result of which is to replace *Lactobacillus* auto strains to the probiotic strains in natural habitats of the human body.

Key words: lactobacilli, adhesion, buccal epithelium, erythrocytes

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THE CHANGE IN THE LEVEL OF CYTOKINES IN BLOOD AND SYNOVIAL FLUID IN THE POSTTRAUMATIC PERIOD OF PATIENTS WITH DEFORMING OSTEOARTHRISIS AS CONTINUOUS CHRONIC DISEASE

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The actual problem of the modern approach to the management of patients with traumatic injuries with the purpose of forecasting, prevention and treatment of post-traumatic conditions, is to evaluate in this period, the dynamics of cytokine profile circulating in synovial fluid, and the patterns of their production by mononuclear cells of the victims of this profile.

Material and Methods. In accordance with the purpose and objectives of this study 144 patients with post-traumatic arthrosis (with a history of traumas of a various nature) in age from 23 to 64 years (average age 43,2±5,7) were examined. Out of all examined patients men was 63 (43.7 per cent), women - 81 (56,3%). As the control group, 18 relatively healthy people aged from 30 to 57 years (average age 45,5±4,3) were examined. All of the examined person, depending on the stage of post-traumatic arthrosis, (acute and chronic classification) were divided into 4 groups. The 1st group consisted of 48 patients with 1st stage of deforming osteoarthritis, 2nd - 38

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patients with stage 2nd stage of deforming osteoarthritis, 3-th - 35 patients with 3rd stage of deforming osteoarthritis, 4th - 23 patients with 4th stage of deforming osteoarthritis. Investigations were carried out at the time of hospitalization prior medical interventions. During the research the following methods were used: clinical, physical, instrumental, follow-up, radiation (MRI, CT, R-graphy), endoscopic, laboratory. The synovial fluid from the affected knee was received during medical diagnostic puncture. The definition of Pro-inflammatory cytokines: IL-1, IL-6 and TNF-a in the blood serum and synovial fluid of the knee joint performed by ELISA on the immunofluorescent analyzer Abbott AXSYM" using standard kits ProCon ("Protein contour", St. Petersburg, Russia). Data were processed statistically using Student's t-test.

Results and Discussion. Analysis of the results of determination of IL-1R in the serum of patients DK showed that in all stages of the disease, in addition to IV, the contents of this cytokine exceeded the control values in varying degrees of severity. The highest levels of IL-1R in blood serum was revealed in patients with 1st stage of deforming osteoarthritis. Then downwards in the following order : in patients with 2nd , 3rd and finally, 4th stage of disease on average, respectively, he was $234,4 \pm 12,4$; $198,7 \pm 16,6$; $88,2 \pm 6,15$ (in all cases $p < 0.05$) and $47,4 \pm 4,45$ PCG/ml. While the levels of IL-1R in the serum of patients with the 1st stage of the disease was 4.0 times; stage 2 - 3.4 times; the third stage is 1.5 times higher than in control. And only in patients with stage 4 of deforming osteoarthritis contents IL-1R did not differ from the control. A similar pattern was observed when determining the contents of TNF-a in the serum of patients with deforming osteoarthritis, and only in contrast to the level of IL-1R in patients with 4th stage of deforming osteoarthritis contents of TNF-a remained significantly higher than in control. So, the content of TNF-a in patients with of deforming osteoarthritis of the I, II, III and IV stage of disease on average, respectively, amounted to $330,7 \pm 24,5$; $210,5 \pm 17,3$; $123,4 \pm 15,3$ and $98,5 \pm 12,7$ PCG/ml (in all cases $p < 0.05$)

Conclusion. The results obtained in a comparative study of contents of proinflammatory cytokines (IL-1, IL-6 and TNF-a) in the blood serum and synovial fluid at various stages of deforming osteoarthritis showed that the determination of the spectrum of cytokines in the hearth of the pathological process, in our opinion, is the most perspective and can be a key marker for early detection of damage and organizations of the active preventive measures of deformation processes in the joints in the early post traumatic period of the accident victims, mainly affecting the lower limbs.

Key words: cytokine interleukin (s), tumor necrosis factor, synovial fluid, deforming osteoarthritis

ІМУНОЛОГІЯ (IMMUNOLOGY)

АССОЦІАЦІЯ ПОЛІМОРФІЗМА ГЕНА C159T РЕЦЕПТОРА CD14 И АНТИЕНДОТОКСИНОВОГО ІММУНІТЕТА У ПАЦІЕНТОВ С РЕФРАКТЕРНОЇ/КОРТИКОСТЕРОИД-ЧУВСТВИТЕЛЬНОЇ АСТМОЇ Бисюк Ю. А., Курченко А.И., Кондратиук В.Е., Дубовой А.И.

ASSOCIATION OF POLYMORPHISM OF C159T GENE OF CD14 RECEPTOR AND ANTIENDOTOXIN IMMUNITY IN PATIENTS WITH REFRACTORY / CORTICOSTEROIDS-SENSITIVE ASTHMA

Bisyuk Yu.A., Kurchenko A.I., Kondratiuk V.E., Dubovyi A. I.

Introduction. The refractory asthma refers to the phenotype, which is characterized by severe persistent course with frequent exacerbations and resistance to corticosteroid therapy. This phenotype of asthma can be related to C159T polymorphism of CD14 receptor gene

Material and methods. There were studied the C159T polymorphism of CD14 gene in 331 patients with bronchial asthma. The control group consisted of 285 healthy individuals of Crimea. The C159T gene polymorphism of CD14 was detected by allele-specific polymerase chain reaction with electrophoretic detection. The distribution of genotypes was checked according to the law of the Hardy-Weinberg equilibrium by using Fisher's exact test and χ^2 . There was used logistic regression to determine the difference in the frequency of genotypes and alleles.

Results and discussion. In our study have been identified 291 patients with corticosteroid-sensitive and 40 with refractory asthma. The genotype distribution of control (CC – 34%, CT – 51%, TT – 15%) and patients with corticosteroid-sensitive asthma (CC – 29%, CT – 53%, TT – 18%) were in accordance with the law of Hardy-Weinberg equilibrium and did not significantly differ ($\chi^2 = 2.204$, $P = 0.332$). There were no significant differences when comparing the allele and genotype frequencies by using risk allele T and C model. In the control group the frequency distribution of genotypes CC – 34%, CT – 51%, TT – 15% did not differ significantly ($\chi^2 = 3.540$, $P = 0.170$) from refractory asthma (CC – 52%, CT – 35%, TT – 13%). The risk analysis for the T allele showed that the frequency of CT+TT genotype in patients with refractory asthma (49%) was significantly lower (OR = 0.467, CI = [0.240-0.910], $\chi^2 = 5.17$, $p = 0.023$) compare to control (66 %). In turn, the difference of allelic frequencies for the control and patients with persistent asthma did not differ significantly ($p = 0.076$). The content of anti-endotoxin antibody of class A in patients with corticosteroid-sensitive asthma in serum and induced sputum did not differ significantly ($p > 0.05$) from control. The anti-ET-IgM was significantly higher (< 0.001) in the control group for all genotypes, while genotype TT contents of this immunoglobulin was significantly higher ($p < 0.05$) compare to CC genotype. The concentration of anti-ET-IgG for the studied genotypes was significantly higher ($p < 0.05$) compare to the control group. Patients with TT genotype had the highest content of sCD14 in serum and induced sputum, which was significantly different ($p < 0,05$) compare to control values and CC+CT genotypes. Levels of Anti-ET-IgA and anti-ET-sIgA in patients with refractory asthma did not differ significantly ($p > 0.05$) from control group. The content of anti-ET-IgM and serum sCD14 in patients with CC and CT genotypes were significantly higher ($p < 0,05$) compare to control and did not differ significantly ($p > 0,05$) for TT genotype ones. The concentration of anti-ET-IgG and sCD14 in induced sputum was significantly higher ($p < 0,05$) compare to control, but did not differ between genotypes.

Conclusion. In a population of Crimea the risk of refractory asthma significantly reduced (OR = 0.467, CI = [0.240-0.910], $p = 0.023$) in the presence of CT or TT genotype of C159T polymorphism of CD14 receptor gene. The corticosteroid-sensitive asthma patients with TT genotype of CD14 receptor had high concentration of anti-endotoxin IgM and sCD14.

Key words: bronchial asthma, endotoxin, C159T polymorphism of CD14

ОСОБЛИВОСТІ ПОРУШЕНЬ ГУМОРАЛЬНОЇ ЛАНКИ ІМУНІТЕТУ У ХВОРИХ ХРОНІЧНИЙ ТОНЗИЛІТ ПРИ НАЯВНОСТІ ЦУКРОВОГО ДІАБЕТУ ТА ЇХ КОРЕКЦІЯ Вдовіченко Н.І., Тупотілов О.В., Бойко А.А., Коляда О.М.

CORRECTION OF HUMORAL IMMUNITY DYSFUNCTIONS IN PATIENTS WITH CHRONIC TONSILLITIS AND DIABETES MELLITUS

Vdovichenko N.I., Tupotilov O.V., Boyko A.A., Kolyada O.M.

In the therapy of various forms of chronic tonsillitis (CT) were used as immunomodulatory agents Respibron and Licopid. Diabetes mellitus type 1 (also known as type 1 diabetes, or T1DM) is one of the important factors that could significantly complicate the therapy

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of chronic tonsillitis. T1DM is a form of diabetes mellitus that results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. The aim of our study was to explore the dynamics of immunologic indicators during the active disease and treatments in patients with various forms of chronic tonsillitis, including tonsillitis complicated with T1DM.

Materials and methods. 64 patients with various forms of chronic tonsillitis in active period of disease observed during the study. Patients were divided into the following groups: 21 persons with the compensate form of CT (CTC), 24 persons with the decompensate form of CT (CTD) and 9 persons with the decompensate form of CT complicated with T1DM (CTD+T1DM). The control group consisted of 15 apparently healthy persons. Concentrations of sIgA and IgA in the oropharyngeal secret were determined by the method of radial immune diffusion by Mancini. Lysozyme content was determined using the test system "Lysozyme" ("Reakompleks", Russia). Levels of lactoferrin and SLPI in the oropharyngeal secret of patients were evaluated using ELISA test systems of "BioChemMack", Russia. Patients of group CTC were divided into subgroups CTC1 and CTC2, depending on the applied treatment. Both subgroups treated with standard therapy for two weeks, on the fifteenth day of therapy patients of subgroup CTC2 received Respibron 10 days by 1 tablet once a day and Licopid during 10 days by 1 mg once a day. Similarly patients of group CTD were divided into subgroups CTD1 and CTD2. Patients of subgroup CTD2 received therapy according to the scheme of CTC2. Patients of group CTD+T1DM divided into subgroups CTD1+T1DM and CTD2+T1DM. Patients of subgroup CTD2+T1DM received therapy according to the scheme of CTC2. The effectiveness of the treatment was assessed by the general state of the patients according to oropharyngoscopy and humoral immunity after 45 days of observation. Statistical analysis of the results was performed using the Mann-Whitney U test. According to the accepted level of reliability index value between the groups (p), which constituted or were less than 0.05.

Results and discussion. As a result of immunological studies, it was determined that the exacerbation of chronic process in oropharyngeal mucosa is characterized by immunological failure, such as reduced levels of sIgA, IgA and IgG in the oropharyngeal secret. Content of SLPI in patients with CT before treatment was significantly below control values. Lysozyme level before treatment was significantly reduced in groups CTD and CTD+T1DM. Lactoferrin level was increased in groups CTC and CTD, but in group CTD+T1DM it was reduced. According to our study, patients with CT combined with diabetes had reduced levels of sIgA, IgA, lysozyme, lactoferrin and SLPI, but elevated levels of IgG. After standard therapy content of almost all measured parameters in experimental groups differed from controls. The level of sIgA was reduced relative to control group and before treatment. IgA level was reduced in the group CTD1+T1DM relative control, but significantly higher relative indicators before treatment in groups CTD1 and CTD1+T1DM. The level of IgG in groups CTC1 and CTD1 was increased relative to control group and in groups before treatment. In the group CTD1+T1DM levels of IgG were decreased relative before treatment, but were higher than the control. The level of lysozyme after standard therapy did not differ from the control except group CTD1+T1DM and was significantly higher than the corresponding values before treatment in all groups. The level of lactoferrin in groups CTC1 and CTD1 did not differ from control, but significantly different from the values before treatment. In the group CTD1+T1DM lactoferrin level was reduced relative to control, but had dynamics other than groups without diabetes. In CTC1 and CTD1 groups its level before treatment was increased and after the therapy was decreased, in group CTD1+T1DM we observed the opposite trend. The level of SLPI in all groups was reduced relative to control, but significantly higher than before treatment.

Patients of groups CTC2, CTD2 and CTD2+T1DM in addition to standard therapy on the fifteenth day of therapy received "Respibron" and "Licopid." The level of sIgA in groups without diabetes did not differ from the control group and in group CTD2+T1DM was reduced relative to control, but significantly higher than before treatment and in group CTD1+T1DM that shows the influence of immunomodulatory agents. IgA levels did not differ from the control in all groups. The level of IgG in groups CTC2 and CTD2 was increased relative to control and indicators before treatment, in group CTD2+T1DM IgG levels decreased relative before treatment. Lysozyme and lactoferrin level after treatment with immunomodulators did not differ from controls in all groups. The level of SLPI in groups CTD2 and CTD2+T1DM was reduced relative to control but significantly higher than before treatment. Clinical and immunological evaluation of complex treatment of patients with CT in acute stage by proposed scheme including preparations "Respibron" and "Licopid" and also with T1DM in the anamnesis showed the effectiveness of its use.

Keywords: chronic tonsillitis, diabetes, immunoglobulins, secretory leukocyte protease inhibitor, immunomodulation

КОНЦЕНТРАЦИЯ ЦИРКУЛИРУЮЩИХ ИММУННЫХ КОМПЛЕКСОВ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ГЕНЕРАЛИЗОВАННОМ ВОСПАЛИТЕЛЬНОМ ПРОЦЕССЕ У ЖИВОТНЫХ РАЗНОГО ВОЗРАСТА ПОД ДЕЙСТВИЕМ ИММУНОМОДУЛЯТОРОВ Коваленко Т.И., Климова Е. М., Минухин В.В.

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CONCENTRATION OF CIRCULATING IMMUNE COMPLEXES IN EXPERIMENTAL GENERALIZED INFLAMMATORY PROCESS IN ANIMALS OF DIFFERENT AGE UNDER ACTION OF IMMUNOMODULATORS. Kovalenko T.I., Klimova Ye.M., Minukhin V.V.

Under physiological conditions a formation and a presence of the CEC in liquids is one of the manifestations of the immune response to receipt of antigens and an important factor, which provides immunity. Circulating immune complexes act as agents involved in the regulation of immune response and maintaining communication between the immune system and other regulatory systems of the body and direction to his defense. The intensity of the formation of the CEC may vary under the influence of infectious antigens and immune preparations.

Material and methods. Material for the experiment were white male rats 3 months of age ("young") weighing 100 -140gr. (n = 40) and 22-month ("old") weighing 200 -240 g. (n = 40). And the first (n=10) and second (n=10) groups of rats served as controls. Third (n=15) and fourth (n=15) group of animals was injected intraperitoneal daily agar culture of *Pseudomonas aeruginosa* № 27835 ATCC (injected with 1.5 ml suspension of bacteria, which contained 109 CFU/ml). Fifth (n=15) and sixth (n=15) groups of animals were injected intraperitoneally daily agar culture of *Escherichia coli* number 25592, ATCC (injected with 1.5 ml of bacteria suspension which contain 109 CFU/ml). Control animals were taken from the experiment by decapitation 3rd day - n=20. Control and infected animals were taken from the experiment by decapitation at 3rd day - n=27, 5th day - n=27 and 7th day - n=26. In the second phase of the experiment Ia (n = 6) and IIa (n = 6) were the control group of rats following administration of the experimental composite preparation consisting amino acids, nucleotides, enzymes, vitamins (MF). In two age groups of animals with inflammation induced by E. coli suspension treated with MF 20 mcl 3-month rats (IIIa group n = 6) and 40 mcl 22-month rats (IVa group n = 6). Ib (n = 6) and IIb (n = 6) were the control group of rats after the injection of comparison, containing mannitol and natural antioxidant betakaroten (PO). In two age groups of animals with inflammation induced by E. coli suspension treated with PO 0,5 ml 3-month rats (IIIb group n = 6) and 1 ml 22-month rats (IVb group n = 6). Control animals were taken from the experiment by decapitation on 3rd day - n = 12. Infected animals were taken from the experiment by decapitation on 3rd day - n = 12 and 7th day - n = 12.

Results and discussion. One of the biological functions of the immunoglobulins is neutralization antigens to form circulating immune complexes. In the work it was shown that the induction of inflammation of *P.aeruginosa* and *E.coli* suspension in experimental animals of two age groups led to the increase of the CEC in serum compared to control animals. After administration experimental composite preparation comprising amino acids, nucleotides, enzymes and vitamins (MF) in young animals with inflammation induced by *E. coli* suspension was revealed an increase the CEC, compared with an older group of animals throughout the experiment. When adding formulation containing mannitol and natural antioxidant betacarotene (PO), in the animals two age groups intensity CEC formation depended on the sequence of adding of suspension *E. coli* and immunomodulator PO. Was revealed elevated levels of CEC only, in those

animals which immunocorrector PO was given to induce an inflammatory response.

Conclusion. In the control group of animals older age (22 months) the CEC concentration was 2 times lower than in the young (3 months) control animals. After the action of bacterial suspensions *P.aeruginosa* and *E.coli* formation CEC intensity was significantly increased in both age groups of experimental animals, indicating the activation of antigen binding immunoglobulin infection. The action of the immunocorrective composite peptide drug MF significantly inhibited the formation of the CEC only in older animals throughout the experiment. With the addition of immunocorrector PO revealed increase of the CEC in young and old animals to induce inflammatory of bacterial suspension *E.coli*.

Keywords: immune complexes, generalized inflammatory process, immunomodulators

ОГЛЯД КЛІНІЧНИХ ВИПАДКІВ МЕДИКАМЕНТОЗНИХ АЛЕРГІЧНИХ РЕАКЦІЙ У ХВОРИХ НА ГОСТРІ РЕСПІРАТОРНІ ЗАХВОРЮВАННЯ

Сидорчук А.С., Богачик Н.А., Сокол А.М., Венгловська Я.В., Костіна Н.В.

REVIEW OF CLINICAL CASES OF DRUG ALLERGIC REACTIONS IN PATIENTS WITH ACUTE RESPIRATORY VIRAL INFECTIONS

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Introduction. Problem of drug-induced allergic reaction is especially actual both in well-developing countries as well as in countries of Eastern European region. By the WHO data, distribution of allergy is up to 30 %, and main reasons for that are increasing of pharmaceuticals consumption by a person, change of nutrition style towards more chemicals synthetic substitutions. Generally, a quantity of Europeans with allergy reach 150 mln. Reactions of hypersensitivity to medications is so serious discussion question among physicians and their patients, since it is the most important reason to stop treatment and for refuse remedies. Authors hope, that presenting here clinical material will bring benefit both clinicians and patients like cases of drug-induced allergic reactions due to self-prescribed treatment (antipyretics, antibiotics). Thus, this research paper aimed to analyze the clinical cases of drug-induced allergy in patients with acute respiratory illnesses, which had admitted to Infectious diseases department of Municipal Clinical Hospital of Chernivtsi city (Ukraine).

Materials & Methods. Descriptive clinical study enrolled six clinical cases of drug-induced allergy in male patients admitted in different time to the Infectious Diseases Department of Municipal Clinical Hospital of Chernivtsi city (Ukraine) with clinical manifestation and epidemiological data of acute respiratory viral infections. Mostly cases of drug-induced allergy confirmed by the indirect immune-termometry for determination of role of a drug.

Results & discussion. First case in male 52 years old patient with signs of polymorphic exudative erythema induced by pills against common cold named «Coldflu». Patient had manifestation clinical features of acute respiratory viral infection and was hospitalized to the Department of Droplet infections for detoxicative and desensitization treatment. Within few days his infectious problem had solved, nevertheless skin rash still need care, and he had referred to Dermatologic dispensary to continue his treatment. Another 48 years old patient presented on a second day of common cold the big spotted rash after once taking of the same drug «Coldflu». He continued to use the drug even oftener and the rash distributed more over all skin covers, and big spots became dark reddish and with cyanotic tone. Immediately he transferred to the Hospital with chief complaints on dyspnea, high-grade fever 39°C, and general weakness. Objectively: severe state, he has a few ulcers 0.2-0.3 mm on mucous membranes of oral cavity. His skin over trunk fully covered with generalized rash elements elevated over surface. His treatment included prednisolon 60 mg i/v, enterosorbent, detoxication therapy i/v, gluconate calcium, hepatoprotector per os. Third case induced by aspirin use and characterized by small spotty rash on back and extremities. Three more cases induced by antibiotics consumption: one is in 28 years old male after prescription of amoxiclav by general practitioner – macula-papula rash appeared on hands; two more case induced by ampicillin pills used per os. Generally, the drug-induced allergy the most frequently happens on antibiotics. The finally, biotransformation of drugs and immune pathogenesis is not clear up, but assumed the mentioned above, we may imagine next scenario: for stimulating null T-lymphocytes, dendric cells firstly processing antigen. Later it transported to regional lymph nodes, where antigen must presenting to null T-cells. Antigen-specific T-cells migrates to target organs, and after repeated influence of antigen, they activated and start secreted cytokines that regulated reactions and cytotoxins (granulosin, perforins) which proper lead to tissue damage.

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Conclusions. Thus, problem of allergy is global, self-prescribed treatment and uncontrolled use of medications generally assist for occurrence of drug-induced allergy clinical cases (here «Coldflu», «Aspirin», «Amoxiclav», «Ampicillin»). Important is repeated «meeting» with provoking antigens, as well as role of certain immune dysfunction in patients with acute respiratory viral infection (especially caused by influenza viruses) must be present too. Skin allergy manifestation in described clinical cases include generalized exudative polymorphic erythema, allergic dermatitis of extremities, systemic disorders (dyspnea, hyperthermia, arterial hypotension).

Key words: drug-induced allergy, self-treatment, acute respiratory viral infection, skin rash.

РОЛЬ БАКТЕРІАЛЬНОГО ФАКТОРУ ТА ІМУНОЛОГІЧНИХ ЗМІН ПРИ НЕІНФЕКЦІЙНИХ ЗАХВОРЮВАННЯХ МІКРОБНОГО ГЕНЕЗУ

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THE ROLE OF BACTERIAL FACTOR AND IMMUNOLOGICAL CHANGES IN NONINFECTIOUS DISEASES OF MICROBIAL ORIGIN

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Introduction. Today during the study of the development mechanisms of any somatic disease possible participation of the microorganism as trigger factor or its influence on the course of the disease or development of complications is considered. Microflora participation in the etiopathogenesis of noninfectious diseases allows to divide the latest into the following groups: Naturally, the first aspects of the study of the role of microorganisms in the development of noninfectious diseases are pathological processes developing in the organs and systems of the body, which are natural biotope, particularly gastrointestinal tract. The imbalance in the functioning of the macroorganism (stress, poor diet) causes changes in the composition of endogenous microocenosis and therefore dysbiosis. Thus changes in the hormonal homeostasis, immunoreactivity, in the hypothalamic-adrenal system, speed of peristalsis of the intestines are observed, the overgrowth syndrome in the small intestine develops. A classic disease of a group of diseases that are accompanied by the development of erosive conditions are *Helicobacter pylori* - associated ulcerous disease of 12 duodenal ulcer. Diseases of the colon digestive canal can be divided into 2 groups - ulcerative colitis and tumors. *Escherichia* are the main representatives of facultative anaerobic microflora of the colon and are involved in the pathogenesis of both ulcerative colitis and cancer.

Material and methods. A study in order to compare the inducing impact of *Escherichia* lipopolysaccharide isolated from patients with nonspecific ulcerative colitis (NUC, N=38), Crohn's disease (CD, N=30) and colon cancer (CC, N=38), on the humoral and cellular (cytokine) links of immunity in ulcerative colitis and colon cancer. From the patients in both study groups and individuals from the control group *E. coli* were isolated from fecal for obtaining LPS. Synthesis induction of TNF α , IL-8 and IL-10 was conducted by lipopolysaccharide of own and intact *E. coli* and isolates from control persons.

Results and discussion. LPS isolated from *E. coli* strains isolated from patients with different clinical groups showed varying effects on

the immune response. It was established that cytokines are produced to stimulation by antigens of own microflora more active than by the intact lipopolysaccharide. Moreover, it is typical for both proinflammatory and problastomic cytokines. The highest activity was found in lipopolysaccharide bacteria isolated in patients with Crohn's disease, for the pathogenesis of which immunopathological component was proved and which can accordingly cause certain features of the disease.

Trigger factors for developing reactive arthritis (ReA) microorganisms with obligate (Chlamydia, some viruses) or optional (Yersinia, Shigella, mycoplasma, Campylobacteria, salmonella) parasitism are considered to be. Research of subpopulation spectrum of blood lymphocytes of 20 persons with ReA was conducted. Slight decrease in absolute quantity of natural killers was registered. Thus, the relative index CD16 + 56 + in patients with ReA was $11,8 \pm 1,21\%$ to $14,92 \pm 1,13$ in almost healthy individuals. However, some activation of suppressor affects the immune-regulatory index (IRI). Its amount is 1.74, which generally remains within normal limits, but is 21.8% lower than IRI of control group.

Conclusion. Research of subpopulation composition of T- and B-chains of immunity at ReA to some extent confirm the theory of arthritogenic peptide of the disease development, according to which in the background of T-suppressors activation, induced by microbial triggers, a weakening of cellular immunity occurs, inflammatory reactions with the emergence of autoimmune background develops, that in case of involving muscle and bone system leads to ReA development. In the acute stage of the disease with signs of inflammation it is appropriate to conduct antimicrobial therapy as with ReA and with diseases of the colon also, on the basis of microbiological diagnosis and careful selection of antimicrobial treatment method. New methods of immunomodulating therapy are developed and implemented in practice.

Keywords: ulcerative colitis, Crohn's disease, colon cancer, immunity, *E. coli*

ПАТОГЕНЕТИЧНА ХАРАКТЕРИСТИКА ІМУННОГО СТАТУСУ ПРИ ХРОНІЧНИХ ВІРУСНИХ ГЕПАТИТАХ В І С У ДІТЕЙ

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PATHOGENETIC PROPERTIES OF IMMUNE STATUS AT CHRONIC VIRAL HEPATITIS B AND C IN CHILDREN

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In pathogenesis of chronic viral hepatitis (CVH) B and C in children, there are distinct immune disorders. Purpose: to provide the pathogenic characterization of parameters of cellular and humoral immunity in children with CVH B and C, depending on the phase of viral replication and inflammatory activity.

Materials and methods. An immunological study of peripheral blood of 50 children with CVH B and C, aged 1 to 18 years prior to the appointment of a specific antiviral treatment were conducted. We determined the CD3+, CD4+, CD8+, CD16+, CD22+, CD25+ cell's population and concentration of IgA, IgM and IgG.

Results and discussion. The significant decrease of CD3+ (in 10,3 %) and CD4+ (in 22%) in the phase of viral replication, indicating a persistent shortage of cellular immunity were established. The increase of CD8+ (in 12,5%) indicate the activation of cytotoxic reactions. In patients with the virus in the phase of integration or latent stage population of CD16+ were reduced in 31%, indicating inhibition of cytotoxic responses aimed at the destruction of virus-infected cells. The immune disorders in children with CVH B and C from the phase of viral replication and inflammatory activity in the liver was proven. Since the phase of replication and the increase of the activity of inflammation was an increase of CD8+, indicating activation of cytotoxic reactions and causes progressive destruction of hepatocytes.

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Conclusions: 1. The immune disorders in children with CVH B and C in phase of viral replication are proven. So, there is an increase CD8+, which indirectly indicates the activation of cytotoxic reactions in the phase of viral replication. With the growth of virus replication activity was significantly intensified the ratio of CD4+/CD8+. This proves that in situ populations of CD4+ could positively regulate the activity of CD8+ at CVH B and C. 2. The increase of the activity of inflammation occurs a significant increase in CD8+ and CD16+, which on the one hand contribute to the elimination of the virus from the microorganism, and the other - causing a progressive lesion of hepatocytes as enhance cytotoxicity syndrome are established. 3. Further study of the immune status of children of different age groups with CVH B and C supplement will allow immunopathogenesis of the disease, and improve data pathogenetic therapy of diseases.

Keywords: chronic viral hepatitis B and C, children, immune disorders.

IDENTIFICATION OF EFFECTIVE DILUTIONS OF DENTAL HERBAL REMEDY WITH ANTIMICROBIAL ACTIVITY

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Introduction. There are different ways to solve the problem of resistance of microorganisms. One of them includes an increase of the drug dose, thereby arising adverse reaction, and the other includes a development of the new antimicrobial agents, where no less focus is given to drugs on basis of medicinal plant raw materials owing to the antimicrobial activity confirmed by scientific researches. Herbal remedies are included into treatment codes against infectious and inflammatory dental diseases, however while there is a persistent growth of mouth inflammatory diseases we have signals for expediency of new ones to be produced. Our prior studies deal with developing the tincture conventionally called Casdent, substantiation of using such three types of pharmacopeia medicinal plant raw materials as: licorice roots, sedge cane rootstocks, burnet rootstocks with its roots. The previously determined antimicrobial and antifungal activity of Casdent tincture is insufficient for recommending the use thereof in the therapeutic dentistry, as the external use provides for an additional dilution thereof with saliva, crevicular fluids, exudates.

The aim is to identify the most efficient dilutions of Casdent tincture to substantiate its reasonable application in dentistry.

Materials and methods. Target of examination is Casdent tincture as developed by employees of the Department of General Pharmacy and Drug Safety of the Institute of Pharmacy Professionals Qualification Improvement of the National University of Pharmacy. Control is the herb preparation: Stomatophyt («Phytopharm Klenka S.A.», Poland). The work is performed at the State Establishment «Mechnikov Institute of Microbiology and Immunology of the National Academy of Medical Sciences of Ukraine» through use of museum and clinical strains of microorganisms, which daily cultures have been grown on the respective digest media according to the requirements of the State Pharmacopoeia of Ukraine. The twofold serial dilution method (microbial load has been determined at 0.5 unit as per McFarland scale) has been used. The obtained data of survey are statistically processed according to Student.

Results and discussion. Inhibiting concentration of Casdent tincture diluted in (1:32) has been emphasized in respect to: *S. epidermidis*, *S. pneumoniae*, *B. subtilis* and candida fungi: *C. albicans*, *C. catenulata* (*C. rugosa*) Sclar C-27, *C. albicans* clinical strain No. 23. For strains: *S. aureus*, *S. haemolyticus*, *S. mutans* clinical strain No. 45, *E. coli*, *P. aeruginosa*, the minimal inhibiting concentration value corresponds to dilution of (1:16). Although a similar trend of antimicrobial activity is ascertained at comparing the antimicrobial effect's values of Casdent tincture and those of the control: Stomatophyt, the compared preparation is valid as diluted in (1:32) only in respect to *S. aureus* and *C. albicans*, and in respect to other cultures – as diluted in (1:16). Additional researches of antimicrobial properties of solutions Casdent and Stomatophyt: (1:10), (1:20) have made it possible to identify the minimal inhibiting and bactericide concentration thereof. Based on the level of antimicrobial activity of Casdent tincture it is determined that it is highly competitive with the level of the imported preparation: Stomatophyt, and upon examination of values of bactericide concentration of Casdent dilutions: (1:20) for

S. aureus, *S. pneumoniae*, *B. subtilis*, somehow excels similar dilutions of Stomatophyt.

Conclusion. The effective solutions of Casdent tincture are identified: 1 teaspoonful (5 ml) of Casdent tincture per 100 ml of water – for bacterial static effect and 2 teaspoonfuls (10 ml) in the same volume of water – for bactericide effect. The results of microbiological examinations testify to prospectivity of the developed tincture and will be taken into account when issuing the recommended application thereof in therapeutic dentistry.

Key words: tincture, antimicrobial effect, effective dilutions, therapeutic dentistry.