

Анотації наукових робіт

UDC 616.832-004.2-085.214.31-036.8

**QUALITY ASSESSMENT OF MULTIPLE SCLEROSIS PHARMACOTHERAPY
IN REAL CLINICAL PRACTICE***R.V. Lazor, O.I. Lopatynska**Danylo Halytsky Lviv State Medical University,**Department of Clinical Pharmacy, Pharmacotherapy and Medical Standardization, Lviv, Ukraine*

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The aim of the research: analysis and assessment of pharmacotherapy quality in patients with multiple sclerosis based on Protocols Drug order Forms in order to identify the potential drug related problems (DRP) and elaboration of measures for their prevention and elimination as part of pharmacotherapy improvement in terms of pharmaceutical care.

Materials and methods: objects of the investigations served 36 Protocols Drug order Forms for the patients with multiple sclerosis in a health care institution in Lviv. The evidence based medicine data, the current clinical protocol of multiple sclerosis treatment, international guidelines, National Drugs Lists in Ukraine (issue 5), instructions for drugs use in clinical practice have been used as an information basis for establishment of potential problems of pharmacotherapy of patients with multiple sclerosis. The following methods were used: bibliographic, comparative, analytical, clinical and pharmaceutical, clinical and pharmacological analysis. During the research conflicts of interests were not observed.

Results: Multiple sclerosis is a serious disease of the nervous system, which requires high-cost schemes of immunosuppressive therapy, complete symptomatic treatment, adequate prevention of recurrent relapses, physical, psychological and social rehabilitation of patients, adequate depth of disability, diet, lifestyle changes and self-education. It was established that therapeutic possibilities in multiple sclerosis are different on the profile of risk and benefit. The priority directions for improving pharmacotherapy quality of the disease were determined which could potentially serve as vectors for forming a pharmaceutical care model for patients with multiple sclerosis.

Conclusions:

1. The methodological approaches and basic principles of multiple sclerosis pharmacotherapy were grounded. It was found that simultaneously with high requirements to efficiency, experts and patients put forward high demands for safety of diagnostic, therapeutic and rehabilitation processes that can be achieved only through a personalized approach to treatment.
2. The principal approaches to assessing the pharmacotherapy quality of multiple sclerosis by identifying DRP, determination of their influence on the efficacy, safety and quality of treatment have been elaborated in Ukraine for the first time. It was established that on average 1 patient with multiple sclerosis (1 Protocols Drug order Form) had 5,3 DRP associated with drug use. Only each 4th drug is intended for patients without potential caution. Differentiation of identified DRP allowed to determine the priority of problem solving and vectors of pharmaceutical care.
3. It was proved that the high cost of diagnostic, therapeutic and rehabilitation procedures in multiple sclerosis are serious social and economic problems in Ukraine. In this case, pharmacotherapeutic insurance that requires a differentiated and individualized choice of drugs is significant in the structure of cost. The analysis of 36 Protocols Drug order Forms revealed 166 DRP. Their avoidance can save money, at least 31,24% of the whole pharmacotherapy.

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UDC 614.27:614.8].001.572

**ORGANIZATIONAL AND METHODOLOGICAL PRINCIPLES OF PHARMACEUTICAL SUPPLY SYSTEM
FOR THE POPULATION IN EMERGENCY SITUATIONS***P.V. Olinyk**Danylo Halytsky Lviv National Medical University, Lviv, Ukraine*

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The aim of the research: elaboration and substantiation of organizational and methodological principles of pharmaceutical supply system for the population in emergency situations.

Material and methods: Methods of systemic approach, observation and generalization analysis, synthesis and formalization, simulation modeling were used. The objects of researches were: legislative and regulatory acts related to medical and pharmaceutical supply for the population in emergency situations of peaceful and war time.

ISSN 2070-3112

«Клінічна фармація, фармакотерапія та медична стандартизація»

2014, №1-2

Results: It was determined that the management of system is carried out indirectly, through coordination bonds between governmental organs and elements of the system under current legislation. The current system of the pharmaceutical supply is not capable to fulfill its functions in emergency situations of regional and national level. The main reason of inefficiency is absence of centralized management and subsystem of medicines reserves at national, regional and local levels. The conceptual model of pharmaceutical supply for the population in emergency situations is substantiated in terms of systemic approach.

Conclusions: Organizational and methodical principles of the pharmaceutical supply in emergency situations require renovation of domestic production of immunobiological drugs and basic active pharmaceutical ingredients, normative and legislative decisions on the establishment of a centralized state organs of administration at all levels; creation of reserves system of medicines, products and equipment of medical purposes, sanitary-economic and special properties at all levels; creation of stable levels of reserves of active pharmaceutical ingredients on pharmaceutical enterprises and medical depositories.

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UDC 616-053.51:312.6] (477.83)

COMPARATIVE HEALTH ASSESSMENT OF PRIMARY SCHOOL CHILDREN IN LVIV AND DISTRICTS OF LVIV REGION

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The aim of the research: to determine peculiarities of health status of primary school children in Lviv and Lviv region with further development and implementation of preventive, corrective, sportive and recreative and curative measures.

Materials and methods: the screening survey of 7132 parents of primary school children was performed in Lviv and the following districts of Lviv region: Brodivskyj, Buskyj, Kamyanko-Buskyi and Radechivskyi. Among them: 1st grade schoolchildren – 1771, 2nd grade – 1781, 3rd – 1841 and 4th – 1739. A special questionnaire was developed, containing 50 questions grouped under relevant headings: overview, features lifestyle, physical activity, social conditions, habits, food, a history, including family and others. Heading dealing with prevalence of possible changes in health status of schoolchildren contained 13 questions concerning specific complaints. Statistical analysis of the survey results was performed by means of the program STATISTICA 6 (Statsoft, USA). The method of variation statistics was used. Differences in nominal parameters were evaluated using criteria X². All differences were considered significant at $p < 0,05$

Results: Results of the analysis showed that the majority of parents of primary schoolchildren in Lviv and districts of Lviv region (71,8%) evaluated the status of their children as «healthy», 14,5% – believed that children need medical examination, and 12,7% – indicated that their children need physician's consultation. Only 1,0% of parents evaluated the health of their children as «ill». Therefore, the results of the parents' evaluation of their children health status from Lviv region showed that the majority of parents (71,2%) assessed the state of their children as «healthy», 4,8% – believed that children need examination, and 13,0% – that children require consultation. Only 1,0% of parents evaluated their children as «ill». Regarding the analysis of responses in questionnaires of Lviv citizens, 82,8% of parents said they believe their children «healthy» and only 1,0% – «ill». The results of comparing answers in Lviv and Lviv region showed that 1-4 grades schoolchildren in the Brodivskyj district more often complain on headache (6,5%, $p < 0,05$) in comparison with urban children (3,7%). Complaints on abdominal pain were more frequent in children of Brodivskyj (9,0%, $p < 0,01$) and Kamyanko-Buskyj districts (8,3%, $p < 0,05$) compared to urban schoolchildren (under 5,1%). Complaints on regurgitation were significantly more frequent among primary schoolchildren in Kamyanko-Buskyj (12,4%, $p < 0,01$) and Buskyj districts (11,9%, $p < 0,01$) compared to urban schoolchildren (4,9%). The complaint on cold extremities was more frequent in schoolchildren of Kamyanko-Buskyj (4,9%, $p < 0,05$) comparing to children in Lviv (2,5%). The fact that primary school children in Lviv (8,1%, $p < 0,01$) had more frequent manifestations of allergic reactions compared to children of appropriate age in all investigated areas (Buskyj – 3,1%, Radechivskyj – 3,4%, Brodivskyj – 4,7%, Kamyanko-Buskyj – 4,4%) should be taken into consideration.

Conclusions:

1. According to the subjective evaluation of health status of primary schoolchildren in districts of Lviv region and Lviv, majority of parents (71,8%) identified their children as «healthy» and only 1,0% – as «ill».
2. In Lviv, frequency of subjective assessment of children as «healthy» was 1,16 times higher compared to districts.
3. The most common complaints in primary schoolchildren include: headache, feeling cold in the extremities and signs of pathological disorders of the gastrointestinal tract, which were significantly more frequent ($p < 0,05$) in pupils of Lviv region and signs of allergic pathology – in pupils of Lviv ($p < 0,01$). In our opinion, these pupils need additional laboratory and instrumental investigations, advisory opinions of pediatric specialists with further preventive and, if necessary, treatment measures.

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UDC: 616.31:615.322

STUDY OF A THERAPEUTIC EFFECT OF A DENTAL TINCTURE «KASDENT» ON A MODEL OF STOMATITIS IN RATS

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The aim of the research: was to investigate the therapeutic effect and efficiency of a new medicine developed by scientists of National University of Pharmacy (Kharkiv, Ukraine) – a dental tincture «Kasdent» containing alcohol extracts (40%) of three plants: Burnet rhizomes and roots, Acorus calamus rhizomes and Licorice roots.

Materials and methods: the experimental stomatitis was induced by a single 5-second application of cotton swab with sodium hydroxide solution 10% on the mouth vestibule between the lower lip and mandible incisors of rats. The experiment was conducted on 24 male rats with weight 170-190 g. Animals with induced stomatitis were divided into 3 groups: group 1 – reproducible animal model of stomatitis – positive control; group 2 – animals in which the model-based dental pathologies have been treated with a tincture «Kasdent» (s.06.07.12); group 3 – in which the model-based dental pathologies have been treated with a tincture «Fitodent» (the private joint stock company «Red Star», Ukraine, s. 090912). The group of animals – intact control, has been formed for the control over disease and the therapeutic effect of the drug.

Results: the investigation of the effectiveness of a new dental tincture «Kasdent» has been conducted due to hematological, biochemical, histological parameters. It has been found that tincture helps to reduce the severity or to eliminate symptoms of stomatitis. It is significantly more effective than «Fitodent» tincture.

Conclusion:

1. The application of a damaging factor on the mucous membrane of mandible vestibule in rats caused morphological changes in the tissues characteristic for chronic degenerative and inflammatory processes that turn into systemic inflammation.
2. The treatment with a dental tincture «Kasdent» promoted the normalization of hematological and biochemical parameters, reduced severity of destructive and inflammatory changes and more rapid healing of oral mucosa.
3. The therapeutic effect of «Kasdent» tincture in studied experimental model exceeded the therapeutic effect of «Fitodent» tincture.

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UDC: 615.03:615.276(477.44)

CHARACTERISTICS OF PHARMACOTHERAPY COMPLICATIONS OF NSAIDs ADMINISTRATION DUE TO SPONTANEOUS REPORTS IN PODOLSK REGION IN 2013

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The aim of the research: to study peculiarities of clinical manifestations of side effects caused by administration of diclofenac, ibuprofen, meloxicam and nimesulide with various indications for medical use and to determine their safety profile.

Materials and methods: report forms on adverse events or lack of drugs efficacy (form 137/o). Clinico-pharmacological and comparative analyses have been used in investigation.

Results: 1213 report forms on adverse drugs events have been received from different medical institutions of Podolsk region in 2013.

ISSN 2070-3112

«Клінічна фармація, фармакотерапія та медична стандартизація»

2014, №1-2

We selected only those report forms where suspected drugs that caused the side effects were diclofenac, ibuprofen, meloxicam and nimesulide. The largest share in the total number of selected non-steroidal anti-inflammatory drugs (NSAIDs) makes ibuprofen that caused 45% of all side effects, 40% adverse events were caused by diclofenac, 9% – by nimesulide and 6% – by meloxicam. Adverse reactions of NSAIDs administration appeared the most frequently in women (60% and more of cases). The non-selective NSAIDs (especially diclofenac) were prescribed for all age groups of patients in comparison with the selective ones which have been prescribed in the majority of cases for patients aged from 31 to 60 years. The main indications for NSAIDs administration in the majority of cases were rheumatic (rheumatoid arthritis, osteoarthritis, Bechterew disease, etc.) and non-rheumatic (osteocondrosis etc.) diseases. The allergic reactions in case of ibuprofen administration make 75% of all systemic adverse events, diclofenac – 66,7% nimesulide – 40% and meloxicam – 33,3%. The gastrointestinal disorders formed the next group of systemic adverse reactions, observed in case of diclofenac prescribing in 23.8% and nimesulide – 40%. The cardiovascular disorders were noticed rarely, and primarily in case of selective NSAIDs administration.

Conclusions:

1. The largest number of reported adverse events in Podolsk region was identified in case of non-selective non-steroidal anti-inflammatory drugs administration, such as ibuprofen and diclofenac.
2. The allergic reactions and gastrointestinal disorders are the most common systemic adverse events of the studied non-steroidal anti-inflammatory drugs.
3. The identified adverse events indicate the necessity of careful use of non-steroidal antiphlogistics, especially in patients with diseases of the digestive system, kidneys, circulatory system, central nervous system, allergic history, considering the benefit/risk correlation.

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UDC 616.-008.9:612.397:616.379-008.65]-053.2

LIPID METABOLISM IN CHILDREN WITH INSULIN RESISTANCE AND LEPTIN SIGNIFICANCE FOR ITS REGULATION

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The aim of the research: to study the peculiarities of lipid metabolism in children with insulin resistance and leptin significance for its regulation.

Material and method: Lipid metabolism in 53 children with insulin resistance and 135 children with normal tissue insulin sensitivity were studied. Anthropometry, fasting basis immune reactive insulin, fasting basis glucose, total cholesterol, high density, low density and very low density cholesterol, triglycerides, leptin, indexes HOMA-IR and Caro, non-high – density cholesterol, total cholesterol/high density cholesterol ratio, triglyceride/high density cholesterol ratio, atherogenic index were estimated.

Results: Metabolic insulin resistance was identified in 43 (22,8%) children from 188 examined children, in 21 (30,9%) children from 58 overweight children, 22 (42,3%) from 52 generally obese children, in 27(41,5%) from 65 abdominally obese children. Nonendocrine insulin resistance was estimated in 3 (13,6%) children from 22 children with essential arterial hypertension. Physiological insulin resistance was identified in 7(14,9%) children with normal body mass and arterial blood pressure. It was determined that lipid metabolic changes in children with insulin resistance had the tendency for total cholesterol increase on 2,5%, low density cholesterol increase on 10,8%, triglycerides on 7,8%, non-high-density cholesterol on 11,2% and sensitively increase of high-density cholesterol. Carbohydrate metabolism in children with insulin resistance according to immunoreactive fasting insulin, indexes HOMA-IR and Caro was sensitively associated with blood lipids – high-density cholesterol, low-density cholesterol and very low density cholesterol, triglycerides, total cholesterol/high density cholesterol ratio, triglycerides/high density cholesterol ratio, atherogenic index. Leptin concentration in the children of the 1 group was 1,9 times higher than in children of the 2 group (p=0,002). Sensitively high correlation was estimated between leptin and lipid metabolism: fasting insulin (p=0,70; r=0,0001), HOMA-IR (p=0,71; r=0,0001), total cholesterol (p=0,36; r=0,001), high density cholesterol (p=0,43; r=0,001), non-high density cholesterol (p=0,41; r=0,002), total cholesterol/high-density cholesterol (p=0,29; r=0,03), atherogenic index (p=0,33; r=0,014).

Conclusions:

1. Lipid metabolism in children with insulin resistance is characterized by proatherogenic changes with tendency for atherogenic fractions increase and high density cholesterol sensitively increase as the compensative mechanism for proatherogenic fraction quantity decrease.

2. Leptin in children with insulin resistance is likely to have positive regulative influence on carbohydrate metabolism with increase of insulin sensitivity and decrease of insulin resistance and lipid metabolism normalization with proatherogenic cholesterol fractions decrease and high density cholesterol increase.

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UDC 616.61-008.64-085.38:612.339.1]-085.456.1

THE CLINICAL AND PHARMACEUTICAL ASPECTS OF DIALYSIS THERAPY

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The aim of the research: to study the clinical and pharmaceutical aspects of dialysis therapy.

Materials and methods: The sources of medical and pharmaceutical information; the analysis of scientific literature, data grouping and systematization.

Results: This article reviews the clinical and pharmaceutical aspects of dialysis therapy. Among the clinical aspects are the classifications of chronic kidney disease (CKD), types and modalities of dialysis therapy, the Ukrainian patients distribution suffering CKD for indexes of calcium and phosphate ions. Among the pharmaceutical aspects are the composition of solutions for dialysis therapy, their quality attributes. There are three methods of renal replacement therapy (RRT): a donor kidney transplantation, haemodialysis, peritoneal dialysis. The choice of the RRT method depends upon clinical state of a patient, the possibility of a hospital to provide treatment including state funding. For purpose of conducting effective dialysis therapy it is very important to choose optimal parameters of dialysis for the correction of water and electrolyte balance disorder, azoth homeostasis: dialysis modality, dosage, duration, frequency, solution composition.

Conclusions:

1. The morbidity rate increase in chronic kidney disease causes the topicality of research on the development of solutions for haemodialysis, peritoneal dialysis.
2. It is necessary to carry out constant monitoring of patients' plasma electrolyte composition and to administer appropriate dialysis solutions for the correction of disorder of water, calcium, phosphor balance and acid-base balance.
3. The various dialysis solutions available for price are needed to provide effectively the patients suffering CKD with dialysis therapy. These solutions have to be differed in electrolytes content, the type and concentration of buffers and osmotic agents. The level of availability of dialysis solutions may be improved by means of the implementation of different compositions solutions in the domestic pharmaceutical manufacture.

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ISSN 2070-3112

«Клінічна фармація, фармакотерапія та медична стандартизація»

2014, №1-2

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UDC 615.03:33: 614.2:616-08-039.78

THE CONDUCTING OF A PHARMACOECONOMIC ANALYSIS AT THE CARDIO-THERAPEUTIC DEPARTMENT

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The aim of the research: to conduct a pharmacoeconomic analysis of prescribed pharmaceutical preparations for patients with cardiovascular pathology with further determination of rational pharmacotherapy and ways of its optimization.

Materials and methods: Lists of medical prescriptions (LMP) for patients with cardiovascular pathology (n=50); pharmaceutical preparations (n=145), listed in LMP; the frequency method, pharmacoeconomical analysis, ABC, VED-analysis and matrix ABC/VED-analysis have been used in the investigation.

Results: Pharmacoeconomic analysis of medications prescribed for patients with cardiovascular disease has been conducted. The methods for optimizing drug therapy of cardiac patients are suggested based on the obtained results of the pharmacoeconomic analysis. The role of the clinical pharmacist in the rationalization of the medicament cost has been defined.

Conclusions:

1. The obtained results reveal the irrationality of cost distribution for medications purchase due to significant costs of medications intended for additional pharmacotherapy in comparison with basic therapy.
2. A considerable part of the prescribed pharmaceutical preparations are expensive. But there is no information about their proved effectiveness, in particular with cardiovascular pathology. Consequently, their prescription is not substantiated.
3. The investigation outcomes enable to suggest the following methods for cardiac patients pharmacotherapy optimization: cost reduction for group D medicines, prescription decrease of group D pharmaceutical preparations due to the withdrawal of medications that are not necessary for patients at this stage of treatment; optimization of medicines quantity (in particular, the reduction of the trade names number) including information about the evidence-based clinical efficiency and bioequivalence of generic medications.
4. In our opinion, involvement of clinical pharmacists in conducting pharmacoeconomic analysis will promote the medicine cost rationalization for in-patients therapy, especially at cardio-therapeutic department.

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UDC 615.012.1:547.655.6.076

BIOORGANIC SYNTHESIS OF GLYCOSYLATED ANTHRAQUINONE DERIVATIVES. PART 2. SYNTHESIS OF ALIZARIN DERIVATIVES.

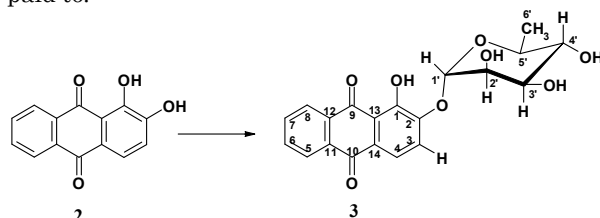
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The aim of the research: Development of methods and obtaining by bioorganic synthesis of glycosylated alizarin derivatives using the soil bacterium of the strain culture *Saccharothrix espanaensis*.

Materials and methods: Monitoring the progress of the reactions and the identification of compounds were carried out by TLC on plates «Merk Kizelgel-60F254» and «Silufol UV-254». Preparative chromatography was performed on silica gel brand «LS 5/40» (Merck). Spectra of ¹H and ¹³C NMR, COSY, HSQC, HMBC, 2D-NOESY, ROESY were recorded on a spectrophotometer «Varian XL-400», «Bruker Avance DRX 400», «JEOL

Alpa», «Bruker WP-200», «Varian XL-200». Chromatography-mass spectra were recorded on «Agilent 1100». In determining the melting temperature correction for speaker connections column of mercury was undertaken.

Results: Glycosylated derivatives of alizarin are widespread in nature **2** and its availability to obtain synthetically led to his selection as an object of research. Bioorganic synthesis was performed by standard methods for a 6-day incubation period. The extract at first of transformational products was analyzed by liquid chromatography-mass spectroscopy, and the formation of new glycosylated anthraquinones corroborated by comparing the UV spectra of initial and final products. Alizarin **2** biotransformed with 87% yield with the formation of four products, the main of which are 2-O- α -L-rhamnozylalizarin (AliPro1) **3** with a yield of 65%; the rest of the formed products were isolated in very small quantities (from 7% to 10%) and significant attention was not paid to.



As evidenced by LC / ESI-MS analysis of the ethyl acetate extract of the reaction mixture with alizarin **2** *S. espanaensis*, major biotransformation product is glycosylated alizarin **3**. Molecular weight of product ion of bioorganic synthesis increased by 145 carbon units, which clearly points to an introduction to the structure of alizarin **2** glycoside moiety - rhamnose to form 2-O- α -L-rhamnozylalizarin (AliPro1) **3** with a molecular weight of 386 carbon units. Thus, the difficulty of synthesis by the classical technique was successfully compensated by bioorganic synthesis using *Saccharothrix espanaensis* strain. It was possible to selectively and with quite good yield to put glycoside fragment into the structure of alizarin.

Conclusions:

1. For the first time glycosylated alizarin derivatives were obtained by biosynthetic way using a strain of bacteria *Saccharothrix espanaensis*.
2. The analysis of data LC / ESI-MS showed that during the biosynthesis a mixture of products with an overall yield of 87% with the formation of four compounds, the main of which are 2-O- α -L-rhamnozylalizarin (AliPro1) **3** with a yield of 65% of the structure which was confirmed by NMR spectra (^1H , ^{13}C , NMVS, H-COSY, ROESY), the rest of the formed products was not allocated because of low yields.

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