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Механізми розвитку патологічних процесів і хвороб та їхня фармакологічна корекція : тези доповідей II Науково-практичної інтернет-конференції з міжнародною участю (21 листопада 2019 р.). – Х. : Вид-во НФаУ, 2019. – 394 с.

Збірник містить матеріали II Науково-практичної internet-конференції з міжнародною участю: «Механізми розвитку патологічних процесів і хвороб та їхня фармакологічна корекція». В матеріалах Конференції розглянуто сучасні проблеми патофізіології: молекулярна та клітинна патофізіологія; роль генетичних факторів у патогенезі захворювань; механізми розвитку патологічних процесів і хвороб; вікова патофізіологія; клінічна патофізіологія; питання викладання патофізіології; фармакологічна корекція патологічних процесів, доклінічні дослідження; лабораторна діагностика; проблеми та перспективи створення лікарських препаратів різної спрямованості дії (лікувально-косметичних, гомеопатичних, ветеринарних, екстемпоральних); оптимізація технологічних процесів створення лікарських препаратів; інформаційні технології і автоматизація наукових досліджень з розробки лікарських засобів; створення нутрицевтичних засобів та виробів медичного призначення; організаційно-економічні аспекти діяльності фармацевтичних підприємств у сучасних умовах; маркетингові дослідження сучасного фармацевтичного ринку; нанотехнології у фармації; сучасна біотехнологія.

Для широкого кола наукових і практичних працівників медицини та фармації.

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Mechanisms of development of pathological processes and their pharmacological correction: abstracts of reports and 2nd scientific and practical Internet conference with international participation (November 21, 2019). – Kh.: NUPh, 2019. – 394 p.

Book of Abstracts includes materials of 2nd Scientific and practical Internet Conference with international participation: «Mechanisms of development of pathological processes and their pharmacological correction». The materials of the Conference consider modern problems of pathophysiology: molecular and cellular pathophysiology; the role of genetic factors in the pathogenesis of diseases; mechanisms of development of pathological processes and diseases; age pathophysiology; clinical pathophysiology; teaching of pathophysiology; pharmacological correction of pathological processes, preclinical research; laboratory diagnostics; problems and perspectives for the development of drugs with different mechanism of action (therapeutic cosmetic, homeopathic, veterinary, extemporal); optimization of technological processes for the creation of drugs; information technologies and automation of scientific research on the development of drugs; creation of nutraceutical and medical products; organizational and economic aspects of the activity of pharmaceutical enterprises in modern conditions; marketing researches of the modern pharmaceutical market; nanotechnology in pharmacy; modern biotechnology.

For a wide audience of scientific and practitioners of medicine and pharmacy.

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ЗМІСТ

THE MISBALANCE BETWEEN PRO-INFLAMMATORY IL-1β AND ANTI-INFLAMMATORY IL-4 IN PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS

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Introduction. Efficiency of local application of medical drugs in periodontal tissues depends on the display of substances in the periodontal pocket (PP), choice of medical substances, method of his application, contact with the gingival oral mucosa and maintainance of this concentration. Therefore it is necessary advantage to give to the forms and pathways of medications with the controlled and long action. Development and application high-efficiency and safe facilities of drug therapy of chronic generalized periodontitis (HGP) the last years legally considered one of priority directions of native and foreign researchers. Medical local therapy is inalienable part of complex treatment of HGP.

Liposomes, owing to their small size, penetrate regions that may be inaccessible to other delivery systems. Cytokines play a major role in inflammatory and immune responses in periodontal tissues the patients with HGP. The misbalance between pro-inflammatory IL-1β and anti-inflammatory IL-4 mediators as being the cytokines for which there is the most substantial evidence for having a central role in cytokine networks in periodontal diseases.

Anti-inflammatory properties of «Lipoflavon» (JSC „Biolek", Kharkov), which contained lecithin liposomes and quercetin are conditioned by his expressed anti-leukotrienes activity. Quercetin inhibits production of inflammation-producing enzyme 5-lipoxygenase (LOX). The immunomodulating action of Quercetinum is known. Quercetinum differentiated regulates expression genes of Th-1 (IFNγ) and Th-2 (IL-4) of cytokines by the normal mononuclear cells of peripheral blood. Quercetinum increased of phenotypical expression of IFNγ mononuclear cells of peripheral blood and suppressed IL-4 are positive mononuclear cells of peripheral blood, that is compared with the results of determination of mRNC/protein.

Therefore the comparative study of changes of pro-inflammatory IL-1β and anti-inflammatory IL-4 cytokines presents considerable theoretical and practical interest for local treatment the patients with HGP of initial-I degrees of severity with gel from the granules of Quercetinum (GQ) and liposomal Quercetinum-lecithin complex (LQLC).

The purpose of study was to increase of efficiency of complex treatment the patients with HGP of initial-I degrees of severity with gel from the granules of GQ and liposomal LQLC due to the correction of cytokine levels.

Material and Methods. The 35 patients with HGP of initial-I degrees of severity were observed. In accordance to treatment all patients were divided into 2 groups: I group – basic treatment with local application LQLC (18 patients) with the use of individual periodontal delivery tray; II group (group of comparison) – basic treatment with local application of gel from GQ (17 patients) with the use of individual

periodontal delivery tray. The control group (C) included 14 healthy subjects without systemic inflammatory disease.

The patients of basic group was conduct base therapy with the local application LQLC (injection form of «Lipoflavon») as a suspension, prepared ex tempore, containing 137,5 mgs of lecithin and 3,75 mgs of Quercetinum. This suspension prepared at a premix 1/4 parts of content of small bottle with 5 ml 0,9% solution of natrium chloride, warmed-up to 380. The patients of comparison group was conduct base therapy with local application of gel from GQ with the use of individual periodontal delivery tray during 40 minutes 2 times per a day to 10 days.

All observed patients in the morning were conducted of mouth liquid (ML) before treatment and through 1, 6 and 12 months after treatment for immunological researches. Through 6 months of patients examined, inspected the condition of periodontal tissues and conducted supporting therapy, which included the professional hygiene of mouth cavity and local treatment using of individual periodontal delivery tray with gel from GQ and LQLC during 10 days for 40 minutes 2 times per a day, and also reception inward during 1 month of 1 g «Granules of Quercetinum» 2 times per a day.

Results and discussion. The patients of control group was mean IL-1β – 64,44 ± 6,2 pg/ml and anti-inflammatory IL-4 - 243,5 ± 17,48 pg/ml. As such, numerous GCF constituents have been characterized to identify biomarkers that may be used to monitor the initiation and progression of gingival inflammation and the immune response.

The first mediators to have their role related to HGP pathogenesis were innate immunity cytokines produced after microbial recognition, such as IL-1β. These cytokines are produced by both resident cells (i.e. epithelial cells and fibroblasts) and phagocytes (i.e. neutrophils and macrophages) in periodontal environment. While the exact contribution of each cell type remains to be elucidated, previous studies described that a hyper-reactive phenotype of phagocytes is related to increased pro-inflammatory cytokines production in HGP.

Recent evidence also points to important roles of resident cells in periodontal bone loss, since the periodontal ligament fibroblasts and osteoclast precursors contact synergistically increases the expression of genes related to osteoclastogenesis, such as IL-1β.

IL-1β is produced by a wide range of periodontal tissues and immune cells and, as such, is considered to have multiple roles in innate and adaptive immune responses to plaque bacteria which feature in the pathogenesis of periodontitis. IL-1β acts (often in synergy with TNF-α and prostaglandin E2 (PGE2)) to induce many of the vascular changes associated with inflammation and in particular to regulate neutrophil emigration from the circulation into the periodontium. In adaptive immunity, IL-1β stimulates antigen presentation by APCs and influences T-cell development and phenotype. Studies of the expression of IL-1β, TNF-α, and PGE2 in oral fluids and periodontal tissues in periodontal disease endorse the important role of these mediators in pathogenesis and, critically, this is supported by the results of investigations of their effect in animal models (including key studies using cytokine antagonists).

Thus, IL-1β, TNF-α, and PGE2 will all activate osteoclast activity, MMP secretion, and alveolar bone resorption in chronic periodontitis.

During the past decade numerous investigators have shown altered cytokine production in periodontitis and attemped to elucidate their role in periodontal diseases. For example, several studies have demonstrated that localized absence of IL-4 in diseased periodontal tissues is associated with periodontal disease activity and progression. IL-4 has been asssociated to control other inflammatory diseases, such as periodontitis. In addition, there is a relative absence of IL-4-producing T cells at sites of inflammation.

The patients with initial-I degrees of severity in the basic group before treatment was mean IL-1β - 123,2 ± 4,94 pg/ml, that was upper than 91 % in the C groups and anti-inflammatory IL-4 - 220,9 ± 11,89 pg/ml, that was lower than 9 % in the C groups. The patients in the comparison group before treatment was mean IL-1β - 122,6 ± 5,2 pg/ml, that was upper than 92 % in the C groups and anti-inflammatory IL-4 - 219,1 ± 7,74 pg/ml, that was lower than 10 % in the C groups.

The patients with initial-I degrees of severity in the basic group after treatment through 1 month was mean IL-1β - 63,44 ± 3,03 pg/ml and anti-inflammatory IL-4 - 316,2 ± 10,73 pg/ml, that was lower than 30 % in the C groups. The patients in the comparison group after treatment through 1 month was mean IL-1β - 76,65 ± 5,21 pg/ml and anti-inflammatory IL-4 - 359,9 ± 10,36 pg/ml, that was lower than 48 % in the C groups.

The patients with initial-I degrees of severity in the basic group after treatment through 6 month was mean IL-1β - 73,09 ± 6,97 pg/ml, that was upper than 15 % in the C groups and anti-inflammatory IL-4 - 292,2 ± 20,77 pg/ml, that was lower than 19 % in the C groups. The patients in the comparison group after treatment through 6 month was mean IL-1β - 85,22 ± 4,75 pg/ml, that was upper than 11 % in the C groups and anti-inflammatory IL-4 - 261,7 ± 16,25 pg/ml, that was lower than 17 % in the C groups.

The patients with initial-I degrees of severity in the basic group after treatment through 12 month was mean IL-1β - 68,57 ± 5,07 pg/ml, that was lower than 1 % in the C groups and anti-inflammatory IL-4 - 289,9 ± 10,91 pg/ml, that was upper than 1 % in the C groups. The patients in the comparison group after treatment through 12 month was mean IL-1β - 84,04 ± 4,17 pg/ml, that was lower than 6 % in the C groups and anti-inflammatory IL-4 - 244,8 ± 16,53 pg/ml, that was lower than 6 % in the C groups.

Conclusions. The research in question demonstrates lipoflavon capability to normalize homeostasis of the oral cavity, normalize misbalance of cytokines in periodontal tissues, thus retarding process of inflammation and destruction of tissues and improving reparation of periodontal structures. High therapeutic efficiency of the liposomal quercetin-lecithin complex for patients with chronic generalized periodontitis, especially that of initial-I degrees of severity was shown to be determined by anti-inflammatory, immunomodulating and periodontoprotecting effects. This allows to recommend lipoflavon for local application as pathogenetically substantiated drug in treatment of generalized periodontitis.