SOME ASPECTS OF CHRONIC RHINOSINUSITIS SAFETY TREATMENT: MICROBIOTA, BIOFILMS, AND LONG-TERM MACROLIDES

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Introduction. The pathophysiology of chronic rhinosinusitis (CRS) is multifactorial. One of the links in CRS pathogenesis is the state of the microbiota. The nature of the interaction between the microbiota and the local immune system is very complex and not fully understood. The role of microbiomes in CRS is difficult to define due to the difficulties of laboratory methods. Biofilm includes any syntrophic consortium microorganisms in which cells stick to each other and are attached to the surface of the nasal mucosa and paranasal sinuses, become embedded within a slimy extracellular matrix and have a three-dimensional structure and are «cities for microbes». Microbes form a biofilm in response to various factors, for example, exposure of planktonic cells to subinhibitory concentrations of antibiotics. A cell that switches to the biofilm mode of growth undergoes a phenotypic shift. In CRS, multiple bacteria have been implicated including *Staphylococus aureus, Pseudomonas aeruginosa, Haemophilus influenza,* and *Moraxella catarrhalis*. Staphylococus aureus biofilms have the greatest association with severe recurrent and persistent cases of CRS (antigen-producing ability). Long-term antibiotic treatment was defined as the duration of treatment over four weeks. The effects of long-term low-dose macrolides are associated with immunomodulation and can be manifested by a decrease of inflammation markers, changes of mucus viscosity, lower levels of IgE and more (for example, 12-week treatment with roxithromycin at 150mg daily). However, one should be aware of the potentially increased risks of cardiovascular events.

Aim. To assess how well ENT physicians and ENT surgeons are informed about the criteria of chronic rhinosinusitis safety treatment with long-term macrolides.

Materials and methods. The practical study was conducted as part of the master's thesis «Clinical and pharmacological analysis of macrolides in chronic rhinosinusitis treatment» as an analysis of doctors' questionnaires, in one part of which criteria for the safety use were presented.

Results and discussion. We have developed a comprehensive questionnaire to assess various aspects of CRS management. «Chronic rhinosinusitis safety treatment with long-term macrolides» section included the the main questions such as «What side effects of macrolides do you know?» and «What patient’s selection criteria do you use when prescribing long-term macrolides?».

When analyzing the questionnaires, the following results were obtained.

Most often, ENT specialists pointed to such side effects of long-term macrolides as dysbiosis (more than 85% of all respondents) and dyspeptic disorders (60% of all respondents). Only 2% of all respondents indicated the possibility of developing such a rather rare but severe side effect as drug-induced QT interval prolongation (long QT syndrome) associated with the potentially deadly rhythm, Torsades de Pointes. It is necessary to focus on this, since CRS patientsvery often have such comorbid pathology as CV disorders. None of the interviewed ENT specialists used such a simple and accessible instrumental examination method as electrocardiography as a safety criterion for long-term macrolides. Also, none of the interviewed ENT specialists focused the attention of patients on the risk of developing such a side effect. However, none of these respondents could indicate the correct name for this side effect (most often called «cardiotoxic effect») and its clinical manifestations.

Conclusions. Long-term macrolides in chronic rhinosinusitis treatment is still a viable option in a select group of patients. However, ENT specialists are not sufficiently aware of the safety criteria for the long-term use of this group of antibiotics. The pharmacist have to be inform all treatment process participants about the safety criteria.

ORGANIZING CLINICAL TRIALS OF MEDICINES DURING PANDEMIC COVID-19

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Introduction. In the last decade, the field of clinical trials (CT) has demonstrated a tremendous pace of development with the introduction of innovative technologies and forecasts of further rapid growth. Thus, in 2019, the volume of the global CT market was estimated at about 42.3 billion dollars USA, and, according to various estimates, should have increased more than one and a half times by 2026.

Aim is analyze the influence of emergency due to COVID-19 pandemic on development of new approaches for CT organization.

Materials and methods. Web-site CinicalTrials.gov, guidelines of regulatory agencies, results of researcher's surveys and science articles.

Results and discussion. The researchers encountered a large list of obstacles associated with COVID-19. Thus, the key risks in an unfavorable epidemic situation, which are in the area of researcher's responsibility, relate to the safety of the subjects of the study, the safety of personnel and the direct activities of the research site and CT processes.

Thus, the continued participation of CT in the traditional mode entails an increased risk of infection for the subjects due to the increased number of contacts and violation of physical distance. Switching CT to remote mode with video visits and other forms of remote monitoring can lead to insufficient control and assessment of the patient's health (increased likelihood of complications, adverse events, etc.). Suspension and cancellation of CT has a negative effect on subjects receiving direct therapeutic benefit from the use of the study treatment.

The staff of the study site is also in an area of increased risk due to increased contacts, additional workload in the mode of change and adaptation of CT activities (additional procedures, their change). Many non-COVID-10 CTs have been threatened with continuation due to the reorientation of financial resources and the prioritization of research into the prevention and treatment of coronavirus infection. Changes to quarantine research sites and modalities include suspension, increased duration of CI, risks of data loss and confidentiality, difficulties in recruiting and enrolling patients, and delivery of study drugs and other materials.

Conclusions. Despite all the unexpected difficulties and difficulties during COVID-19, the CT market is recovered and growth. New remote technologies for CT organization have developed rapidly and implemented in practice.