ISSN 2181-3187

THE ROLE OF RENGALIN IN CHRONIC BRONCHITIS

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Abstract. Chronic cough declines quality of life and increases risk of complications in patients with chronic obstructive pulmonary disease (COPD). Reducing cough severity and associated negative effects is important therapeutic goal in COPD. Rengalin is a release-active combination antitussive drug based on antibodies to bradykinin, to histamine and morphine. It acts at various mechanisms of cough reflex by modifying endogenous target molecules and their interaction with receptors. The drug's efficacy, as demonstrated previously in experimental and clinical studies, is mediated by specific release-activity obtained as a result of the production process.

Keywords: rengalin, anti-inflammatory activity, codelac, chronic bronchitis, bradykinin, receptor

Introduction. Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by an irreversible or partially reversible obstruction of airways, primarily due to chronic inflammatory pulmonary response caused by the effect of noxious particles or gases. COPD is a progressive disease, which leads to worsening of patient's quality of life (QoL): decreased tolerance of physical activity, limitations in everyday life, increased cough, shortness of breath, and sleep disturbances. The prevalence rate of this disease in the world at the end of 2019 was 384 million cases. COPD causes the deaths of 3 million people annually. According to the study conducted by Wacker et al (2017), average annual per patient costs for COPD treatment in Europe were 7263 €. The high comorbidity of COPD increases the risk of severe complications, worsens the prognosis, and raises the cost of treatment.

The main symptoms of COPD include shortness of breath, cough, sputum production, wheezing, and chest tightness. The prevalence of symptoms varies depending on patient population and disease severity. Chronic cough is frequently the first symptom of COPD, and it is underestimated by patients and considered to be an expected consequence of smoking and/or an environmental effect. Apart from maintenance therapy, which is aimed at achieving COPD control, concomitant treatment is important, and it is directed to improve patient's QoL, including through the treatment of cough. With COPD, as with other chronic respiratory diseases, it is

ISSN 2181-3187

crucial to manage the cough. Cough management involves the rational use of drugs blocking the cough reflex and/or optimizing the sputum removing.

Recently, it was revealed that high dilutions of any substance obtained using a technological process, namely by a repeated dilution of the original substance in combination with an external physical impact, have an ability to modify the activity of the original substance. High dilutions should be considered as a product of technological processing of the original substance rather than its small dose. It has been established that the trigger mechanism of action of high dilutions is their ability to exert changes on conformation of the original substance/target molecule.

The efficacy and safety of the high dilutions have been clinically proven in numerous studies conducted in accordance with the evidence-based medicine.

Rengalin for cough treatment (OOO NPF MATERIA MEDICA HOLDING) with anti- and protussive activity is manufactured on the base of technologically processed antibodies to bradykinin (anti-B), histamine (anti-H) and morphine (anti-M). The active components of Rengalin modify the ligand–receptor interaction of bradykinin, histamine, and endogenous opioids with their receptors.

According to in vivo studies, anti-B reduces the number of cough episodes caused by capsaicin and citric acid. Anti-H modulates the activity of H1, H2 and H3 receptors, reduces peripheral vascular permeability, bronchial smooth muscle spasm, mucus production, and histamine liberation. Anti-M targets are coughing reflex centers. Due to the complex influence of all components, Rengalin affects the central and peripheral pathways, regulates cough, and also decreases the swelling and exudative inflammation, which provides a broncholytic effect, and relieves a sputum expectoration.

This article presents the results of the clinical trial performed to evaluate the efficacy and safety of Rengalin for treatment of cough in patients with stable course of COPD.

Methods. Efficacy and safety assessment of rengalin in the treatment of cough induced by acute upper respiratory tract infections (URIs) in comparison with a complex codeine-containing drug (codelac) was performed as part of a multicenter, randomized clinical trial involving 143 patients. All the participants presented with dry/non-productive cough caused by URIs (pharyngitis, laryngitis, tracheitis, tracheobronchitis, bronchitis). The duration of cough varied between 12 hours and 7 days. Rengalin was administered in 73 patients receiving 2 tablets 3 times daily for initial three days, and half reduced doses--for the subsequent four days; codelac was administered in 70 patients who were given 1 tablet 3 times daily for the entire treatment period (7 days). Primary efficacy endpoints were time to cough resolution and reduction in the severity of the cough (scored using a Cough Severity Scale).

Results. The antitussive effect of rengalin was significantly comparable ($p < 0.025$) with that of codelac; the time to complete resolution of cough (both daytime and nocturnal) was 7.2 ± 1.0 days (versus 7.0 ± 1.1 in the group of codelac). Rengalin's efficacy was evidenced by a sufficiently reduced cough severity in the initial few days after treatment onset. As a result of the entire 7-day treatment, the severity score was reduced by 3.1 ± 09 (versus 3.1 ± 1.0 in the group of codelac; $p < 0.05$), totaling 0.2 ± 0.5 point in both groups at the end of the administration period. The frequent non-productive/dry cough was fully resolved in 76% of patients. All the participants in Rengalin group achieved either convalescent outcomes or significant improvement; none of the patients developed secondary bacterial complications.

Conclusions. Rengalin is a new efficacious and safe drug indicated for the treatment of URI-induced cough. The severity of daytime and nocturnal cough begins to decrease as soon as on the first day after rengalin administration, with severity reduction observed throughout the whole treatment period. At the completion of the 7-day administration, cough severity is reduced by almost 100% and its changes are comparable with the outcomes of treatment with codelac. Rengalin is an effective and safe drug in patients with stable COPD and persistent cough, despite stable doses of maintenance therapy according to the GOLD guidelines. Four-week therapy decreases severity of cough by two times in more than 40% of patients.

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